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In the United States District Court
for the District of Kansas

DAVID BURTON,

Plaintiff,

vs.

R. J. REYNOLDS TOBACCO CO., et al.,

Defendants.

Case No. 94-2202-JWL

VIDEO DEPOSITION OF

G. ROBERT DIMARCO, PH.D.

WINSTON-SALEM, NORTH CAROLINA

AUGUST 14, 2001

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In the United States District Court
for the District of Kansas

- - -

DAVID RUNTON,

Plaintiff,

vs.

R. J. REYNOLDS TOBACCO CO., et al.,

Defendants.

Case No. 94-2202-JWL

Video deposition of G. ROBERT DIMARCO, PH.D., taken on behalf of the Plaintiff at the law offices of Womble, Carlyle, Sandridge & Rice, 200 West Second Street, Conference Room 11-A, Winston-Salem, North Carolina, commencing 9:22 a.m., Tuesday, August 14, 2001, before Marion R. Ciccarelli.

Produced by R.J. Reynolds Tobacco Company in Runton v. R.J. Reynolds Tobacco Co., et al.

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I N D E X

WITNESS: G. ROBERT DIMARCO, PH.D.

	PAGE
STIPULATIONS:	7
EXAMINATION	
MR. MCCLAIN	8, 208
MR. MARPLE	199

EXHIBITS

DEPOSITION

NUMBER	DESCRIPTION	PAGE
1 -	"Survey of Cancer Research"	11
2 -	"Research Planning Memorandum on the Nature of the Tobacco Business and the Crucial Role of Nicotine Therein"	13
3 -	"Research Planning Memorandum on some thoughts about New Brands of Cigarettes for the Youth Market"	16
4 -	"R.J.R. Individual Performance Plan"	19
5 -	"Memo to S.B. Witt from T.M. Finnegan"	25
6 -	"R.J.R. Mission Statement on Smoking and Health"	29
7 -	"Can We Have an Open Debate About Smoking"	31
8 -	"Checklist of Areas of Legal/Litigation"	39
9 -	"Proposed Procedure for Legal Review of R&D"	43
10 -	"Memo to S.B. Witt From W.W. Juchatz 12/13/82"	45
11 -	"Handwritten Note 1/31/83"	63
12 -	"Handwritten Note 3/8/23	66

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EXHIBITS (Cont'd.)

DEPOSITION

NUMBER	DESCRIPTION	PAGE
33 -	"March 12, 1983 (draft)"	74
34 -	"R&D Product Research Proposals"	80
35 -	"Memo to S.B. Witt from W.W. Juchatz 4/14/83"	85
36 -	"Re: G.R.D. 4/19/83"	101
37 -	"Working Draft"	105
38 -	"G.R.D. Discussions"	109
39 -	"Memo to Rodgman from Reynolds 9/27/82"	111
40 -	"Memo Mr. Jay Giles RE: Weekly Highlights"	117
41 -	"Implications & Activities Arising From Correlation of Smoke ph With Nicotine Impact"	124
42 -	"Technology Ammoniation"	135
43 -	"Draft Ammoniation, 6/9/82"	137
44 -	"The Health Consequences of Smoking: Cardiovascular Disease - A report of the Surgeon General"	139
45 -	"Memo to Rodgman from Robinson 7/25/83"	154
46 -	"Smoker Compensation"	157
47 -	"Key Issues"	169
48 -	"Proposed Biobehavioral/brand R&D Cooperative Projects"	172
49 -	"Subject: Project X.B."	175
50 -	"Review of X.G.T. technology"	191
51 -	"Reports of Meetings"	192

52649 4152

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EXHIBITS (Cont'd.)

DEPOSITION

NUMBER	DESCRIPTION	PAGE
32 -	"British Baboon Research Exonerates" Coumarin"	208
33 -	"Invalidation of Some Reports in the Research Department"	209
34 -	"Lists of reports"	213

QUESTIONS WITNESS WAS INSTRUCTED NOT TO ANSWER:

PAGE 96, LINE 14

PAGE 103, LINE 25

PAGE 104, LINE 22

PAGE 113, LINE 10

PAGE 113, LINE 23

INFORMATION TO BE SUPPLIED:

(NONE)

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STIPULATIONS

Pursuant to notice to take video deposition, the deposition of G. Robert DiMarco, Ph.D., was taken before Marion R. Ciccarelli, Notary Public and Court Reporter. The deposition was taken at the law offices of Womble, Carlyle, Sandridge & Rice, 200 West Second Street, Conference Room 11-A, Winston-Salem, North Carolina, beginning at 9:22 a.m. on Tuesday, August 14, 2001.

Reading and signing of the deposition was waived.

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VIDEOGRAPHER: The time is 9:22. This begins tape 1 for the deposition of Doctor G. Robert DiMarco. This is being taken in the matter of *David Burton versus R.J. Reynolds Tobacco Company, et al.* This is being heard in the United States District Court for the District of Kansas, Case Number 942202-JWL. The Court Reporter may now place the witness under oath.

G. ROBERT DIMARCO, PH.D.,

having first been duly sworn, was examined and testified as follows:

EXAMINATION

BY MR. MCCAIN:

Q. Doctor DiMarco, would you state your full name, please.

A. G -- Gabriel Robert DiMarco.

Q. And is -- am I right? Is it Doctor DiMarco?

A. Yes, it is.

Q. And do you have a Ph.D. --

A. Ph.D.

Q. -- in a discipline?

A. Plant pathology.

Q. And were you, sir, an employee of the R.J. Reynolds Corporation for a time?

A. Yes, I was.

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Q. What was your position?

A. For a period of time I was Research Director, and then I became Senior Vice-President of Research.

Q. What was the entire tenure of your employment with R.J. Reynolds Tobacco Company?

A. Approximately ten years between '82 and '92.

THE WITNESS: Can you hear me? I'll try.

Q. BY MR. MCCLAIN: Doctor DiMarco, I'm here to take your deposition regarding some of the work you did regarding the manufacture and development of cigarettes.

Were you involved in the research and development efforts of R.J. Reynolds Tobacco Company in regard to cigarette manufacture?

A. From a research point of view, of course.

Q. Now, was the department that you were involved with, throughout your tenure, the Research Department at R.J. Reynolds Tobacco Company?

A. Yes, it was.

Q. When you came to R.J. Reynolds Tobacco Company, what was your position?

A. There was a Senior Vice-President of Research at Reynolds, and I reported to him for approximately a year; and I honestly don't remember whether I was a Vice-President or just a Director of Research at that time.

Q. Can you tell me, sir, who you -- who the

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Senior Vice-President you reported to was when you came to work at Reynolds?

A. Doctor Roy Morse.

Q. Now, we've had depositions in this case of Doctor Senkus and Doctor Rodgman. Did you know both of those men?

A. Senkus, I've met very casually. Rodgman, I knew very well, yes.

Q. And were you a colleague of Doctor Rodgman's in the Research Department?

A. He reported to me.

Q. When you came to work at Reynolds, did you attempt to review the research that had been done at Reynolds regarding cigarette smoking from previous decades?

A. I don't know what you mean by "review," but, obviously, you've become somewhat familiar with what was going on in the Research Department.

Q. Let me ask you, one of the issues that you addressed in your research was the ability of cigarette smoke to cause cancer. Am I right?

A. What we -- one of the -- I'll straighten up in a minute.

One of the things I was interested in was reducing the biological activity of cigarettes, yes.

Q. Let me hand you what we'll mark as Exhibit 1.

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(Plaintiff's Exhibit 1 was marked for identification.)

A. (Reviewing document.) Yes. Is this for him?

Q. BY MR. MCCLAIN: That's for you. Same document. This is a document from 1953 by a Doctor Claude Teague. Did you know Doctor Teague?

A. Yes, I did.

Q. Can you tell me what -- how you knew Doctor Teague?

A. He was part of the Research Department.

Q. Was he someone that was also involved in attempting to reduce the bio activity of tobacco smoke?

A. I honestly don't remember what position Claude had with the company. He was not a -- he didn't have a group with him. So it would be hard for me to -- I just didn't interact that much with him.

Q. Let me ask you to look at this document called "Survey of Cancer Research with Emphasis Upon Possible Carcinogens from Tobacco."

A. Do you want me to read it?

Q. Just -- I'm going -- I'm going to direct you to a page in it. On Page 14 is where -- you can read it. You can read the whole thing, if you'd like, but I'd like to turn your attention to Page 14 -- whenever you're ready. Under the conclusions it says:

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"The increased incidence of cancer of the lung in man which has occurred during the last half century is probably due to the new or increased contact with carcinogenic stimuli. The closely parallel increase in cigarette smoking has led to the suspicion that tobacco smoking is an important etiologic factor in the incidence -- in the incidence -- in the induction of primary cancer of the lung."

Do you see where I am?

A. Uh-huh.

Q. Did you know -- did you know that Doctor Teague had penned such a memo as early as 1953 when you came aboard?

A. No. No, I did not.

Q. What was your interaction with Doctor Teague in the department?

A. I told you I don't remember the position he was in. He didn't report to me directly, as I remember it. And so I just don't remember. He left rather early, I think, in my tenure. I liked him, by the way, but I don't remember exactly what he did.

Q. Let me ask you, were you aware of -- you studied the compound nicotine?

A. Have we studied the compound nicotine?

Q. Have you personally?

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A. No.

Q. Have persons working with you and for you studied nicotine?

A. Absolutely.

Q. Let me hand you what we've marked --

(Plaintiff's Exhibit 2 was marked for identification.)

Q. BY MR. MCCLAIN: This is -- I'm handing you a document which is -- it was also written by Doctor Teague, on the "Research Planning Memorandum on the Nature of the Tobacco Business and the Crucial Role of Nicotine Therein."

Would you look at this for a moment?

A. (Reviewing document.) I'm looking for the date. I found the date.

Q. '72. This is before you arrived.

A. Yeah, could be.

Q. Let me turn you to the first paragraph of the document. "In a sense, the tobacco industry may be thought of as a highly, as being" -- I'm having a hard time. Let me start again.

First paragraph, "In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry. Tobacco products, uniquely, contain and deliver nicotine, a potent drug with a variety of physiological

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effects. Related alkaloids, and probably other compounds, with desired physiological effect are also present in tobacco and/or its smoke. Nicotine is known to be a habit-forming alkaloid, hence, the confirmed user of tobacco products is primarily seeking the physiological satisfaction derived from nicotine and perhaps other active compounds."

What is a physiological active compound?

A. That's a compound which we react to physiologically, which is everything you eat; everything you breathe -- not everything you breathe, but most everything you breathe.

Q. It says -- it says here his -- "Nicotine is known to be a habit-forming alkaloid, hence the confirmed user of tobacco products is primarily seeking the physiological satisfaction derived from nicotine and perhaps other active compounds."

What's -- what is a ---

What would be the physiological satisfaction derived from nicotine? What does that phrase mean?

A. I have no idea. I mean, I didn't write this. I'm a smoker, by the way. I have smoked for many years, but I'm not smoking right now. I didn't smoke for nicotine; I smoked because I enjoyed it.

Q. It says, "His satisfaction of product and pattern of uses are primarily determined by his individual

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nicotine dosage requirements and secondarily by a variety of other considerations including flavor and irritancy of the products, social patterns and needs, physical and manipulative gratifications, convenience, cost, health considerations, and the like. Thus a tobacco product is, in essence, a vehicle for the delivery of nicotine, designed to deliver the nicotine in a generally acceptable and attractive form. Our industry is then based upon design, manufacture and sale of attractive dosage forms of nicotine, and our company's position in our industry is determined by our ability to produce dosage forms of nicotine which have more overall valuable -- value, tangible or intangible, to the consumer than those of our competitors."

Do you see that? Where he wrote that?

A. You just read it to me, yes.

Q. Yeah. Were you -- were you aware that Doctor Teague had taken this position in regard to the nature of the cigarette business before you arrived at R.J. Reynolds Tobacco Company?

A. No, I was not.

Q. Were you aware that Doctor Senkus called him his right-hand man?

A. No.

Q. You didn't know him in that capacity because Doctor Senkus had left by the time you arrived?

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A. No. I said I only knew Doctor Senkus very casually. He's asked to use our library once in a while and I said, "Sure, go ahead and use it."

Q. You knew that he had been in the Research Department --

A. Of course, yeah.

Q. -- before that time.

Let me hand you what we'll mark as Exhibit 3.

(Plaintiff's Exhibit 3 was marked for identification.)

Q. BY MR. MCCLAIN: This is another memo by Doctor Teague from 1973. It's "Research Planning Memorandum on some thoughts about new brands of cigarettes for the youth market." I want to read you the first paragraph of this document also. It says, "At the outset it should be said that there are -- there" -- Oh, I'm having trouble today. Let me start again.

THE WITNESS: Another cup of coffee.

MR. MCCLAIN: I had -- I need something.

Q. BY MR. MCCLAIN: Let me start again with the first paragraph. It says, "At the outset it should be said that we are presently, and I believe unfairly, constrained from directly promoting cigarettes to the youth market: that is, to those in the approximately twenty-one-year-old and under group. Statistics show, however, that large,

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perhaps even increasing, numbers in that group are becoming smokers each year, despite bans on promotion of cigarettes to them. If this be so, there is certainly nothing immoral or unethical about our company attempting to attract those smokers to our products. We should not in any way influence non-smokers to start smoking; rather we should simply recognize that many or most of the '21 and under' group will inevitable -- inevitably become smokers, and offer them an opportunity to use our brands."

Did you know that Doctor Teague had written such a memo before you arrived?

A. No, I did not. No, I did not.

Q. You did receive, did you not, Doctor DiMarco, when you came, a briefing or an orientation by the lawyers for the company?

A. I received a briefingand orientation by marketing people, the lawyers of the company, the manufacturing people. In fact, I demanded that before I joined the company.

Q. And why is that you demanded it?

A. Simply because I was -- I had a pretty good job on my own. I wanted to be sure that I was making the kind of move that was going to be good for me. Quality, that reflects the kind of people you're dealing with, obviously.

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Q. When you said "you had a pretty good job," what was your job before you joined R.J. Reynolds?

A. I was the Director of Research, basic research, or fundamental research for General Foods. Pretty large group in Terrytown, New York.

Q. So when you came, did you meet a fellow by the name of Mr. Witt, the Vice-President and General Counsel for R.J. Reynolds Tobacco Company?

A. Yes, I did.

Q. And did he have a role within the Research Department?

A. What do you mean, "did he have a role within the Research Department"? Did he -- did he run the Research Department? The answer is no.

Q. Did he conduct R&D sensitivity seminars?

A. Tell me what you mean by "sensitivity seminars"?

Q. Well, let me hand you a document --

A. Did we -- did we interact with Legal? Absolutely.

Q. All right. And did Mr. Witt interact with you?

A. Personally? We were both on the Board of Directors. I mean, the Operating Committee together, absolutely.

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Q. Let me hand you exhibit -- what we've marked as Exhibit 3 [sic].

(Plaintiff's Exhibit 4 was marked for identification)

MR. MARPLE: Four.

MR. HALL: Four, I think.

MR. MCCLAIN: Four. Thank you.

Q. BY MR. MCCLAIN: This is a "R.J. Reynolds Tobacco Company 1984 Individual Performance Plan." And this is when you were with the company. Am I right?

A. This is a -- mine says '83, by the way.

Q. Do you see --

A. Do we have the same document?

Q. It says prepared December 1983, but at the top --

A. Okay.

Q. Okay.

A. Uh-huh.

Q. See, it says "1984 Individual Performance Plan"?

A. I just wanted to be sure we had the same document.

Q. We do. And this is from Mr. Witt.

A. Uh-huh.

Q. And it says that --"Acct. Number 1" at the

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A. I suspect that he -- all people in research have all kinds of orientations, absolutely. I never had a problem with that, by the way.

Q. So Mr. Witt --

A. I have a problem when somebody's trying to correct what I do, or what my people do.

Q. And did you have discussions with people within the corporations from time-to-time when you felt like they were directing you to do things that you didn't feel were appropriate?

A. No. As it turns out, you get to know me pretty quick, and we just didn't have the problem. I just made it -- that was clear when I joined the company; that, you know, I am what I am. My record shows what I was and what I've done, and they knew that when he hired me.

Q. Okay. Let me ask you about 1983.

(Plaintiff's Exhibit 5 was marked for identification.)

Q. BY MR. MCCLAIN: This is a document to Mr. Witt from a Mr. Timothy Finnegan. Are you familiar with both those gentlemen?

A. Mr. Witt?

Q. Yes.

A. And Mr. Finnegan?

Q. Yes.

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A. Yes.

Q. How did you know ---

Who is Mr. Finnegan?

A. Mr. Finnegan is a member of the law firm that was used by the corporation.

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company.

(Plaintiff's Exhibit 6 was marked for identification.)

Q. BY MR. MCCLAIN: Let me hand you another document. A 1984 document.

A. (Reviewing document.)

Q. This document is from November of 1984. It's entitled "R.J. Reynolds Tobacco Company Mission Statement on Smoking and Health," and it contains many of the same types of statements that we saw in the last document.

In 1984, was this, as you understood it, the company's position on smoking and health in 1984?

A. I don't have reason to recall whether it was or it was the exact wording, but essentially -- it's essentially what the company believed, yeah.

Q. It says that "There is a significant" -- I'm reading from the third bullet point.

A. Uh-huh.

Q. "There is a significant body of information that is contrary to the hypotheses that smoking causes or contributes to disease causation."

Do you see that?

A. Uh-huh.

Q. And was this, as far as you can recall, consistent with the company's position as of 1984?

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A. Only if you include the parts above it. That -- that's not been proven that.

Q. Yes.

A. Yes, of course. By the way, you should know from a technical point of view, if we knew, man, I'd have an easy job. Just fix it and reduce the risk.

Q. Well, we're going to come to some of those documents where you did some research in that regard.

A. Of course.

Q. That was one of the -- one of the aims that you had in the Research Department, am I right, that you were attempting to discover ways to reduce the risk?

A. Absolutely. But I think you ought to know, and I'm told not to talk about it, but I'm going to tell you anyway. And I've told it -- I've said it many times in public. The company has never objected to it, because that's -- it's my ongoing position. No one has ever proven that cigarette smoke causes cancer.

By that, we mean mechanistically, this product of cigarette smoke does this, this, and this, and produces cancer. No one's ever shown that, but we have never -- and, therefore, hasn't been proven. But we have never ignored the statistics. And so we have always said, and I've always operated such -- I'm really trying to save you some time, like it has been proven.

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It's one thing to say it has not been proven, which it has not; what's important is how you act. We have always acted like it has been proven.

Q. All right. Let me -- that's a very good -- that's a very good -- that's a very good point of -- of departure then --

A. And it makes all this kind of trivial to me.

Q. I understand. I understand your position. Let me then ask you a question about the next document in sequence, Exhibit 7.

(Plaintiff's Exhibit 7 was marked for identification.)

A. I'm having trouble reading this.

Q. BY MR. MCCLAIN: Okay. Let me read it to you.

A. It will take a little bit of time.

Q. It says, "Can we have an open debate about smoking." From 1984. Do you see that at the top, stamped "Received 1984," --

A. Uh-huh.

Q. -- and it says "R.J. Reynolds Tobacco Company."

A. Uh-huh.

Q. It says, "The issues that surround smoking are so complex and so emotional, it's hard to debate them

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objectively. In fact, many of you probably believe there is nothing to debate. Over the years, you've heard so many negative reports about smoking and health -- and so little to challenge these reports -- that you may assume the case against smoking is closed. But this is far from the truth."

Do you see that?

A. Uh-huh.

Q. "Studies which conclude that smoking causes disease have regularly ignored significant evidence to the contrary. These scientific findings come from research completely independent of the tobacco industry. We at R.J. Reynolds think you will find such evidence very interesting because we think and believe -- we think reasonable people who analyze it may come to see this issue not as a closed case, but as an open controversy."

Do you see that?

A. Yes, I do.

Q. Now. Take -- I mean, I'll read the whole document to you, but I'm asking you to --

A. I can read it, if you give me the time.

Q. I will. You state that earlier that you were operating under the assumption that cigarettes caused cancer, whether you could prove it mechanistically or not.

A. What I said to you was -- let's do it carefully now.

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Q. Okay.

A. Is that we did not ignore the statistics. The statistics are out there for everybody to see. Statistics never prove causality. They just don't axiomatically. But you couldn't ignore the statistics. So in my position I convinced the company, and I'm sure it was convinced before that, that we should act like it had been proven. It's the prudent way to do it. I did the same thing, by the way, I had the same job at the food company. Exact -- because the food company has biological activity in everything they sell, too.

Q. I understand. The issue -- the issue is in regard to your previous statement was that you proceeded as if --

A. You know, the prudent way to act was to proceed as if it could cause, not could cause. And the -- and I say we just did not ignore the statistics. No good scientist would.

Q. Do you see anywhere in this -- in this document --

A. I don't care what the document says.

Q. I know. But this was published to the public. Not inside the company. This is what was said --

A. I don't care what the document says. I'm only responsible for what I do.

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Q. I understand. I'm just -- and I'm not -- and I'm not criticizing you, Doctor DiMarco --

A. But --

Q. I'm not -- I'm just trying to establish the facts as your lawyers told you to do in those memos -- remember, just state the facts.

Do you see any discussion here of an assumed link between cigarettes and disease?

A. Of course. As soon as you say it's a controversy. It says just what you just said, yes.

Q. It does. So point me to that language as you -- as you would read it.

A. You just read it. You just said that the cigarette company said that this is a controversy.

Q. Right.

A. As soon as -- as soon as you say it's a controversy, yeah.

Q. It says, "Studies which conclude that smoking causes disease have regularly ignored significant evidence to the contrary."

A. They probably have.

Q. "These scientific findings come from research completely independent of the tobacco industry." Do you see that?

A. No question about that.

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Q. Okay. Do you see any statement in there which says that we in the Reynolds Tobacco Company proceed as if cigarettes cause disease?

A. No. Why would -- why would they say that?

Q. I don't know. I'm just asking you, did they?

A. In this document?

Q. Yes.

A. No, they did not. They certainly have in other occasions, though.

Q. Do you have any published document like this that says that in this 1984 time period or anytime before that?

A. Do I have? No.

Q. Do you --

A. Not that I -- not that I know -- remember.

Q. Okay. We'll -- we'll look -- we'll look at some of the other documents and --

A. It's okay with me.

Q. -- see which ones -- which ones you had a hand in. Now, there's something else you said that I want to clear up before we move on.

A. Sure.

Q. You mentioned bio activity in food products. Is there any food products -- you were at General Mills?

A. General Foods.

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Q. General Foods. I'm sorry. What brought -- what food product did General Foods produce?

A. About three hundred (300) hundred of them.

Q. Just give me one that was very popular.

A. Coffee, Jell-o, whipped cream.

Q. Let's take Jell-o. Lots of consumers of Jell-o?

A. Yes.

Q. Biologic activity in Jell-o?

A. You can register some, yes.

Q. Would --

A. Biological activity in the way it's used in our field, it just means that your body reacts to it. Well, if it has anything in it that you digest, yeah, your body is going to react to it.

Q. Were there -- were there large numbers of people that ate Jell-o that had cancer?

A. Not that I know of.

Q. And there was no link between eating Jell-o and cancer, was there?

A. Not that I know of.

Q. Or any product that General Foods manufactured?

A. Well, now, be careful. They also sold coffee and there's been a lot of controversy around coffee.

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Q. All right. And can you tell me whether or not there were studies which, in fact, linked large numbers of people to drinking coffee and developing cancer?

A. Mostly associated with methylene -- it wasn't methylene chloride. It was another compound used before we used methylene chloride, and I'll think of it in a minute -- as a decaffeinating agent, yes.

Q. All right. And that decaffeinating agent was linked with -- with --

A. Cancer.

Q. -- potential cancer --

A. Yeah.

Q. -- in laboratory animals, not in humans, right?

A. Well, that's right.

Q. Laboratory animals?

A. Yeah.

Q. Okay. And that was taken out of the decaffeinating process then, wasn't it?

A. No. Only after we found a good substitute.

Q. But the answer is, "yes, it was"?

A. It was. But, again, the same -- I had the same position there.

Q. Okay.

A. All we were trying to do is reduce biological

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activity wherever I could. And we took that out for another compound call methylene chloride. And, by the way, that was also accused. And it all comes down to a simple fact that -- Glenious, I think is his name, said it three, four hundred years ago, "the poison is in the dose," which makes everything a poison. Everything.

Q. So is it your position that --

A. Including --

Q. -- that cigarettes -- that cigarettes are no more harmful or potentially harmful than other food products? That's not your position, is it?

A. No. I -- I did not say that.

Q. All right. I just want to be clear. That is not your position?

A. No, of course not.

Q. All right. Doctor DiMarco, in your view, has there been any product that has been more highly associated that's been sold to the American consumer than cigarettes that has been attributed to so many diseases?

A. I don't know. I never asked myself that question. We have certainly removed products from the marketplace that -- that shouldn't have been there. Legally removed, by the way. As far as I know, cigarettes have never been legally removed from the marketplace.

Q. Right.

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A. And those that were legally removed showed a direct causal relationship. And you know what they are.

Q. And in those instances where we have found products that cause death and disease, we remove them generally from the marketplace, right?

A. No, I didn't say that. I said they were removed legally from the marketplace --

Q. And cigarettes --

A. -- and that means that there was good reason to remove it from the marketplace.

Q. And cigarettes have not been.

A. They have not been removed legally from the marketplace, at least -- unless something happened this morning.

Q. Well, maybe. Now. Previously we saw a document about sensitivity training that Mr. Witt had done. Let me show you a document that --

(Plaintiff's Exhibit 8 was marked for identification)

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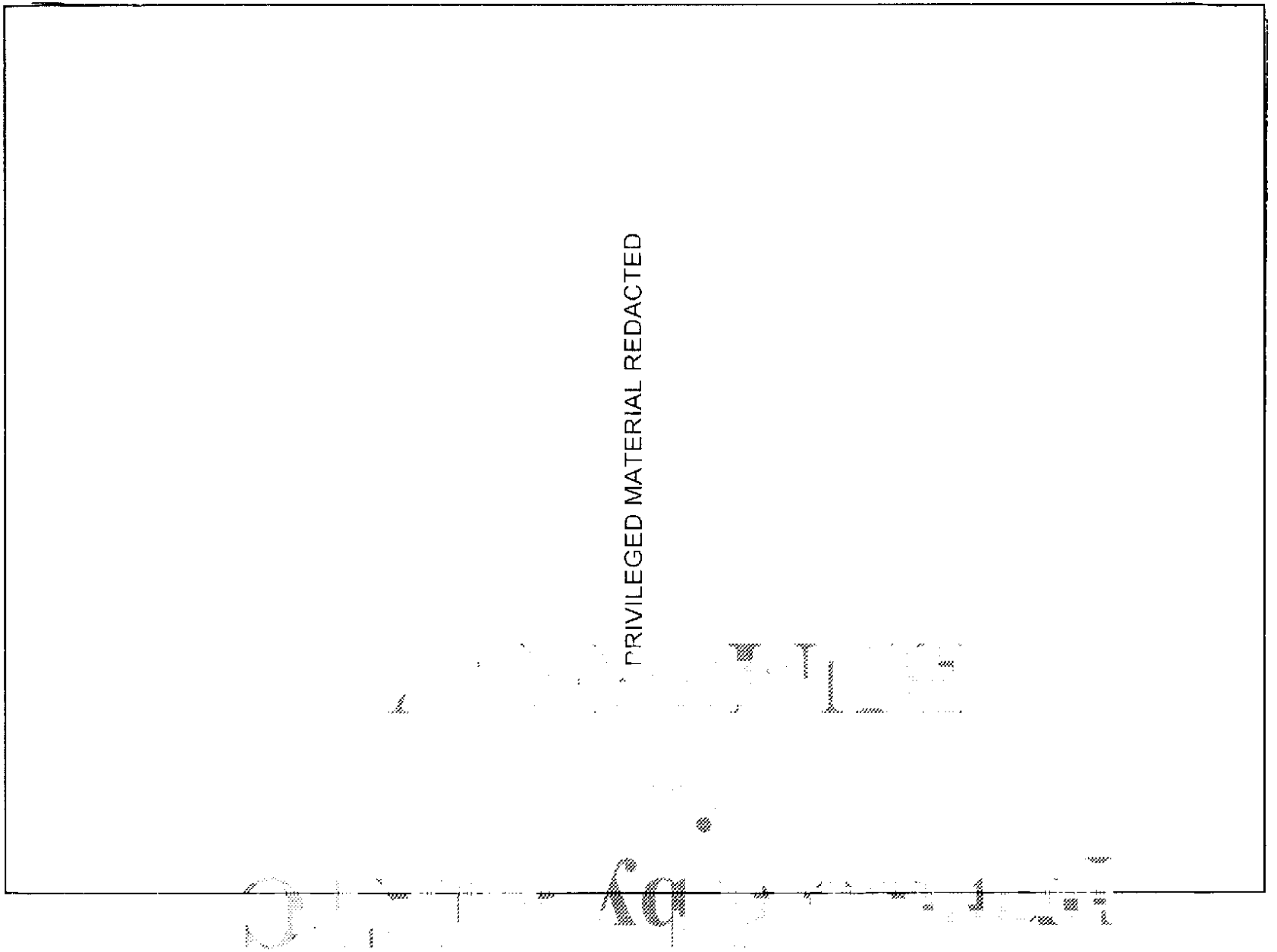

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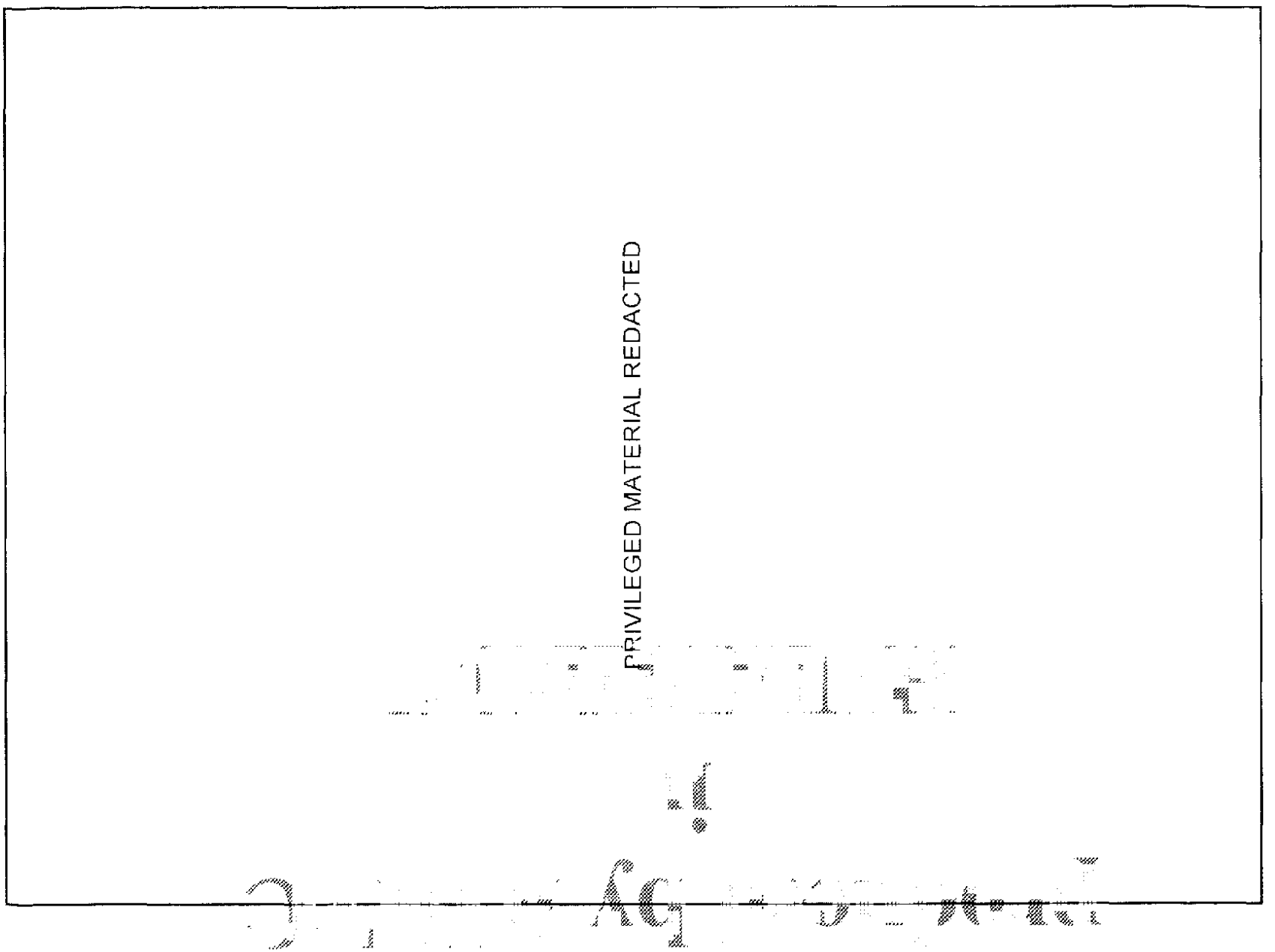

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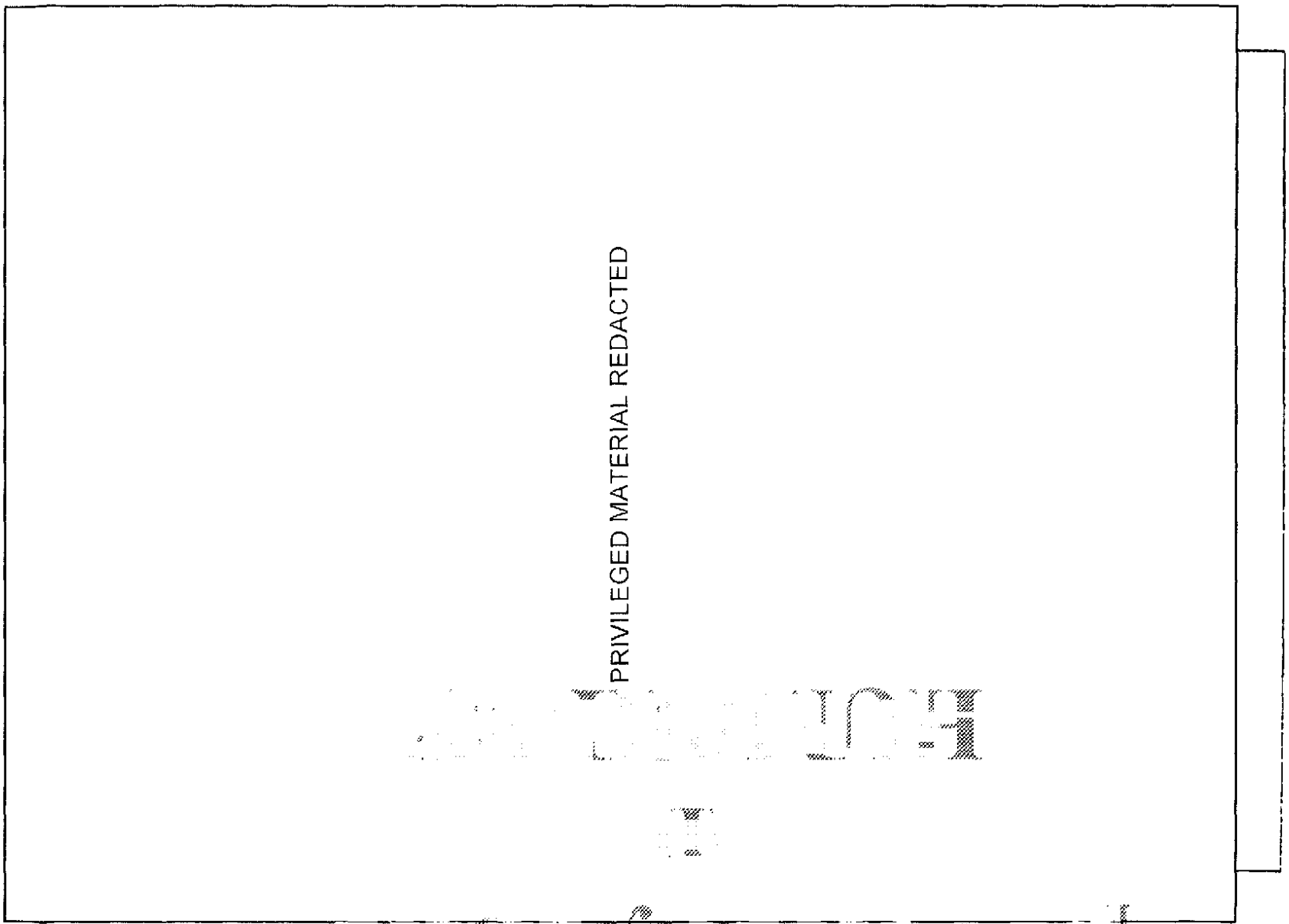

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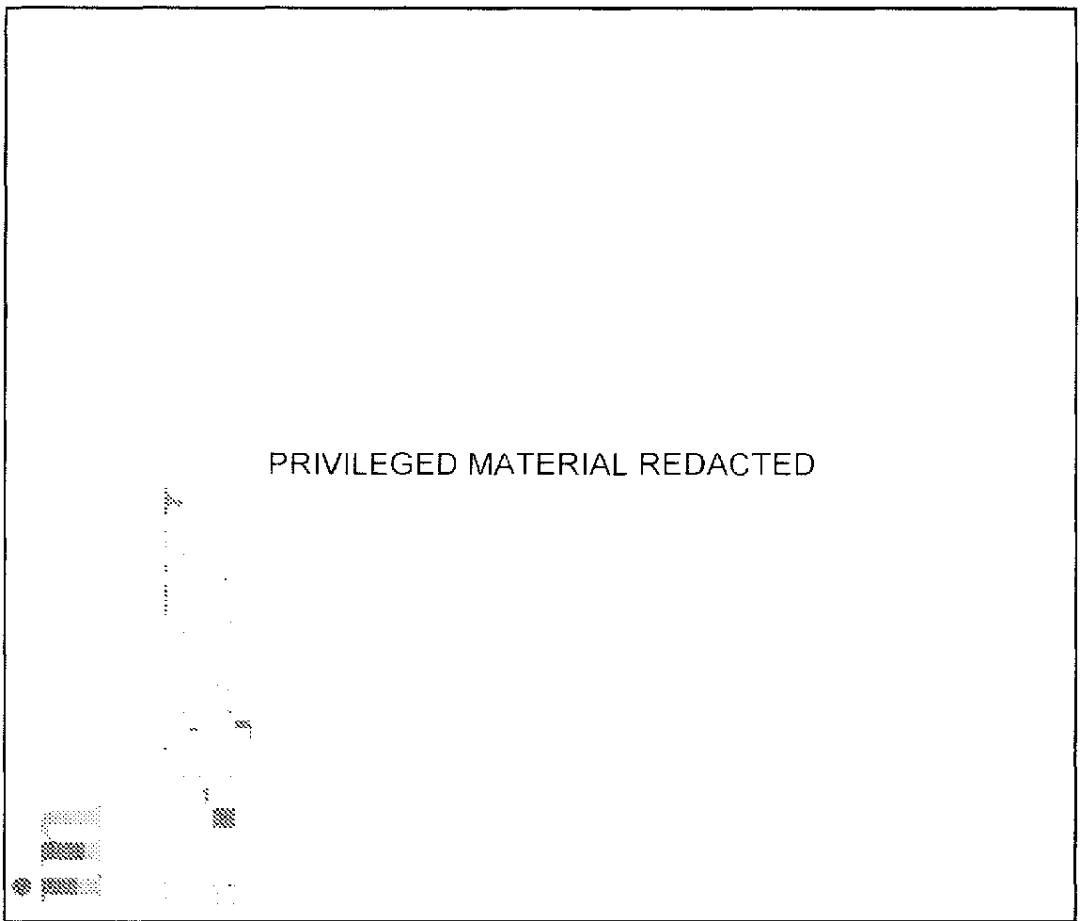

MR. MARPLE: I need to object to that question. I think that that's -- on the grounds of attorney/client privilege, and attorney work product.

Q. BY MR. MCCLAIN: Okay. You can go ahead and answer it.

MR. DAVIS: Well, let me -- let me hear that question again. Read that back to me.

THE WITNESS: Listen, while you fellows are doing this, can I get rid of some coffee?

MR. MCCLAIN: Yeah, sure. Would you like to take a break?

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Buttons Tobacco Archive http://www.industrydocuments.ucsf.edu/docs/xqxl0001

VIDEOGRAPHER: We're off the record at 10:23.

(Video recording was stopped.)

MR. MARPLE: Before you ask your next question, I want to object to the use of Exhibits 8, 9, 10. I don't believe those were ones that you submitted to the court for ruling on privilege or work product protection, and so I object to their use at the deposition and ask that those exhibits be placed under seal in the deposition transcript.

MR. MCCLAIN: They're on the Internet. So, I mean, I'm happy to go about this any way you want. If you want to seek a ruling on this at a later time, I'm happy to do it. I don't know that there's any -- I promise, we're not going to put this in the paper, if that's want you want, but I don't know what putting it under seal for this purpose means.

MR. MARPLE: I say I request we do that to assert our privilege in the case.

MR. MCCLAIN: I agree that you don't waive your -- how's this: you don't waive your privilege claim.

MR. MARPLE: I'll accept that, but I still assert the privileges on these documents, attorney/client, opinion/work product, and want them under seal so they're protected in this deposition record.

Q. BY MR. MCCLAIN: Mr. -- Doctor DiMarco --

MR. MCCLAIN: Are we ready to go back?

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VIDEOGRAPHER: Yeah, for the video, let's just announce the time, so I can start.

MR. MCCLAIN: All right. Go ahead.

VIDEOGRAPHER: Stand by.

MR. MARPLE: Were we on -- did you get our conversation?

COURT REPORTER: Yes.

MR. MARPLE: Okay. Thank you.

VIDEOGRAPHER: On the record at 10:36.

(Video recording recommenced.)

Q. BY MR. MCCLAIN: Doctor DiMarco, do you remember discussing with lawyers your belief about the obligation of a responsible manufacturer of a product that was known to be or suspected to be mutagenic?

MR. DAVIS: Objection.

MR. MARPLE: Let me object to that question as calling for attorney/client privileged information, and I request that the witness not answer the question.

MR. DAVIS: Read the question back to me.

MR. MCCLAIN: Well, let's get away from that problem. Okay, let me ask it a different --

COURT REPORTER: Wait, wait, wait. Let me go forward then.

MR. MARPLE: Let her get --

COURT REPORTER: Go ahead.

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MR. MCCLAIN: Let's get away from the problem.

Q. BY MR. MCCLAIN: Doctor DiMarco, did you have, in this time period, a view about the obligation that a responsible manufacturer of a potentially mutagenic product had to the marketplace?

A. I will now ask you to repeat that because it's obviously an important question.

Q. Yeah.

A. Go ahead.

Q. My question is, in about 1982 when you came aboard with the company, did you have a view about what responsibility a product manufacturer had to the buying public when manufacturing a potentially mutagenic product?

A. I most certainly had a view, but from what you said, and my answer would give you to believe -- might lead you to believe that anything mutagenic could -- would be harmful, that certainly's not true.

We know that some things that are mutagenic in products are beneficial, just the way a vaccine would be beneficial. So I obviously had a view, but before I'd make a decision on anymore specific question, it would have to be -- I have to know more about the product we're talking about. Not so much the product, but the issue that -- that we're discussing.

Q. As it relates to cigarettes, did you have a

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view about what a responsible manufacturer of cigarettes should do in light of their potential mutagenic properties?

A. Again, I answered that question I thought the way I should with the way I felt. I would have to know more about the product in question within the cigarette as to whether it should be handled one way or another.

Q. All right.

A. Simply because all mutagens, as I've said to you, are not harmful. Most everything that you deal with, especially natural products are somewhat mutagenic, but some are very beneficial. In fact, some of them are essential for life, by the way. Selenium is a good example, but mutagenic, we have hundreds of them, by the way -- mutagenic that you better have some or you're not going to live very long.

Q. Were those the products that were predominant in cigarette smoke?

A. Selenium is obviously a product in cigarettes.

Q. And what about the -- what about the harmful mutagen in cigarette smoke? Were there some?

A. Harmful, again, needs more clarification. Things are only harmful at a given level. "The poison is in the dose," as I said to you before.

Q. In the level delivered by a cigarette.

Deposition Exhibit

http://legacy.library.ucsf.edu/tid/jrr07a00/pdf
Studies http://www.industrydocuments.ucsf.edu/docs/xqxl0001

A. I have no way of knowing that.

Q. You have no way of knowing after all your years of research?

A. Now, wait a minute. No way of knowing when you're talking about specifics compounds. If I knew, it would be easy. All you have to do is go in and take it out.

Q. All right. Let's not -- let's not -- maybe I'm not -- I don't want to mischaracterize your statement. As a whole --

A. I'm glad you don't.

Q. As a whole, is it your belief that cigarette smoke contains a combination of harmful mutagen or not?

A. On the whole, cigarette smoke contains mutagens, as does coffee, as does the steak you ate last night, if you had steak. Probably in the same proportions, by the way. Now before you're going to do that, if you want to lower -- because you don't know what else to do, if you want to lower biological activity where the statistics say, "hey, there might be a problem here," the way I suggested we do it is to lower our mutagenicity. I did the same thing, by the way, in other companies.

Q. In the case of cigarettes, their worst statistics which suggested there was a problem with these products. Am I right?

A. Yes.

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Q. In humans. Not just laboratory animals.

A. In humans, of course.

Q. Right. Now --

A. By the way, there's a risk with the steak you ate last night, too.

Q. I didn't eat steak last night.

A. No, I did.

Q. You were better off than I was.

A. Yeah, but I had to cook it myself.

Q. Well, I had to eat it on the airplane. I still think you're up on me. But we'll leave that discussion to the side.

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Q. I'm asking you about, in this point in time, 1982. Do you recall?

A. I can tell you that before this point in time I chaired the National Committee on Food Safety. And we established through that committee and with well, well known names, by the way, that the one hit model, which was developed by a doctor by the name of Doctor Fox, who I personally interviewed, was obsolete, yes.

That is, again, consistent with the "poisons in the dose." When you talk about the one hit model, what you're saying, in effect, is any single molecule can -- obviously the more of them, the more -- the better the chance, but any single molecule could cause some defect. And that's -- that was prevalent.

The man who developed that model was a mathematical model, somebody has it on tape, by the way, because we did interview him. That that's -- that is obsolete.

That now we know that a certain amount of any chemical you have a -- not only a threshold level, and it

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differs from human to human, by the way, or animal to animal before you begin to get an effect. And the effect increases with -- with the dose. In fact, now we know that even at some very low levels you have a very beneficial effect to animals. So that the one hit model was obsolete, yes.

Q. You go on --

A. In my opinion.

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Did you believe at the time that the role of the outside lawyers had restricted the proper functioning of the R&D Department, Doctor DiMarco?

A. The answer is no.

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Q. It said --

A. I could say absolutely, no.

Q. At this point in time, did you have a belief that the Legal Department was preventing you from doing research regarding the benefits of smoking, due to concerns about F.D.A. regulations? Now, this is your belief I'm asking about. Did you believe that?

A. No, I did not.

Q. And do you recall stating it to anyone?

A. No, I do not.

Q. Do you recall at this point in time a discussion regarding ammonia being removed from the list of ingredients you were submitting to the F.D.A.?

MR. MARPLE: Let me object, if you're asking him about the discussion with a lawyer.

Q. BY MR. MCCLAIN: I'm -- I'm recall -- I'm asking do you recall discussions about this subject in general?

A. No, I don't.

Q. Do you recall threatening to quit if that ingredient was removed from the list of ingredients that was submitted to the F.D.A., Doctor DiMarco?

A. I don't recall -- I don't recall any of that. And I have no idea why he wrote it.

Q. Are you saying that it's inaccurate?

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A. I have no idea. I don't recall. You're talking about twenty (20) years ago, by the way.

Q. Doctor DiMarco, there was a submission to H.H.S., Health and Human Services, regarding the list of ingredients in the products of R.J.R. Did you have a role in submitting that list?

A. I personally knew of the list, obviously, but I personally did not make the decision. We had people who were well trained to do that within the department; very well trained.

Q. But do you recall what your role was in regard to that submitted list, if any?

A. I obviously assigned a person who worked with him on what was in the list. I wouldn't even have to assign it. It would go directly to whoever -- you know, whoever took care of that responsibility.

MR. MARPLE: Ken, before you go on, I need to assert another objection, and that's on Exhibit 4. I didn't realize that that was a privileged document. And I want to assert attorney/client privilege and opinion/work product, and ask and request that that exhibit, Exhibit Number 4, also be sealed in the deposition record.

Q. BY MR. MCCLAIN: Doctor DiMarco, I'm going to hand you -- I'm sorry. We'll mark it as an exhibit.

(Plaintiff's Exhibit 11 was marked for

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identification.)

MR. DAVIS: What number is this, 11?

MR. MCCLAIN: 11.

Q. BY MR. MCCLAIN: Doctor DiMarco, this appears to be handwritten notes with you at the top at about the same time -- "Bob D. 1/31/83." Do you see that?

MR. MARPLE: Let me object to the use of this document, if you'll give me just a second. I don't believe this one has been submitted to the court for a ruling. This is a privileged document and I assert attorney/client and opinion/work product as to this document --

Q. BY MR. MCCLAIN: Doctor DiMarco, would you turn --

MR. MARPLE: -- and ask that it be sealed as part of the deposition record.

MR. DAVIS: You're not saying "don't answer the question"?

MR. MARPLE: He hasn't asked one yet. I don't believe -- there's not a question pending, is there?

MR. MCCLAIN: No.

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A. Uh-huh.

Q. Do you recall feeling in the time period January of 1983 that you weren't in control of the R&D Department?

A. No way.

Q. Or that you were highly frustrated?

A. I don't recall, but no way was I not in control. I want you to understand that.

Q. I understand what you're telling me. I'm asking you about in this time period. If you could recall, did you feel like you were in control of R&D Department or were other entities in control of R&D?

A. No, I was in control. I don't recall this at all, but I'm sure I was in control.

Q. Okay. All right. And do you remember feeling highly frustrated at the time about this subject?

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A. I could be highly frustrated about a lot of subjects at any time, but I don't recall this at all.

Q. So --

A. Are you asking me, can I get frustrated, the answer is yes.

Q. Do you remember threatening to leave the firm?

A. I don't know whether I would ever have to say that. The firm would know that if I didn't control my responsibility within the company, then I would go. I mean, they would know that. I wouldn't have to say anything. And they've never disappointed me, by the way, ever. All these things that you're asking me about are memos that I've not seen, we've done.

Q. Doctor DiMarco, in that same time period, do you remember about being very nervous about your job?

A. No way. I don't remember, but I can't say --

Q. Let me see if I can refresh your recollection about that subject.

(Plaintiff's Exhibit 12 was marked for identification.)

MR. MARPLE: Let me object to Exhibit 12 as being attorney/client privilege and attorney work product -- and that is a document that hasn't been submitted to the court

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for ruling in this case, either, and ask that it be submitted and placed under seal as part of the deposition record.

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A. Absolutely fair, but that does not include the fact that whatever they were reporting -- if you're implying that what they're reporting affected what I did, then that would be wrong, because that's certainly not true.

What the company allowed me to do was what I asked to be done, and I just want to make that perfectly clear, I and my peers or people that reported to me. It was an outside advisory group.

Q. Now, after you were done with your research work, however, Doctor DiMarco, it was up to management to decide how to utilize it. Am I right?

A. No way. Before I joined the company -- and I did this, by the way, at General Foods, I didn't have to at the university -- it was very clear that we would publish everything that was publishable during my tenure.

And, by the way, this company, R.J. Reynolds,

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has had lots of stuff in publication. We published long before I got there. But I wanted it clear that everything we did was going to be published. The only holdup -- only two reasons why you wouldn't, one: it wouldn't be worth publishing and that decision was made by scientists; and, two: we would hold up a publication if it involved a patent, until a patent was received.

A patent, by the way, is a publication, and then we would publish it in a referee journal. Totally clear and has never been backed up -- the company has backed me up one hundred percent all the time.

Q. Didn't ask you anything about publication.

A. Yes, you did.

Q. No. I asked you about use of the research that you were doing by the company as in -- as in development of products.

A. No. You didn't say as in development of products. You said "by the company." And "by the company" included, obviously, publications.

Q. Well, if I was unclear about my question, I -- I apologize for that and I'll start again. And I ask that your answer be stricken, because it doesn't relate to what I was trying to ask you about.

What I am asking you about is that after work was done in the Research Department, it would be up to

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management to determine how that research was utilized. Am I correct?

A. No, you're not.

Q. All right. So it was to -- up to Bob DiMarco as to whether or not the work that was done in R&D would, in fact, end up in a product?

A. If, in fact, it proved worthwhile, why wouldn't the company allow it to be used?

Q. Well, I'm asking you, were you responsible for making that decision? Which of the -- which of the discoveries in the Research Department were used or not used? Was that your decision or someone else's?

A. It was Marketing Department's decision.

Q. Okay. That's --

A. It was -- it is every place, by the way.

Q. I'm trying to understand the function here. The work that you did in research was then, what, passed on to marketing for use --

A. No, it was passed on --

Q. -- if --

A. -- it was passed on to Marketing normally, which unless you get specific, I have to answer generally, to evaluate it with consumers.

Q. All right. And so just because you thought that something was beneficial did not necessarily mean that

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it ended up being utilized in a product. Am I right?

A. Well, I don't know that I would take the position to something that's beneficial, until it was proven to be beneficial.

Q. Let's state it this way --

A. I can -- I can -- you know, I take the position, obviously, this is a change.

Q. All right. A change that you would recommend to marketing would not necessarily end up in a product. Am I right?

A. It would not end up in a product that proved not to be not acceptable to the consumer.

Q. All right. And so --

A. It might if it had reasons to.

Q. And so in terms of the functioning of the Research Department, the things that you did in research didn't necessarily end up in products for sale to consumers. Am I right?

A. Well, if you put that in context, you're right, but that would be true of any Research Department in any department throughout the world, yeah.

Q. All right. Well --

A. I just want that in context, because --

Q. Well, you've said that several times --

A. Well --

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Q. And I haven't asked about any other companies, and we're not -- we're not suing any other company. We're here suing R.J.R. Tobacco Company.

A. Yeah, but your question might lead you to believe that this is unique to this company. It's not unique to this company. It's unique -- it's done everyplace the same way.

Q. If you could just answer my question. We have that as a matter of record, and I'm going to ask that it be stricken.

Because I'm asking you about the R.J.R Tobacco Company and I'm asking you how R.J.R. Tobacco Company did it, not what any other cigarette company or any other manufacturer did.

A. But Mr. Counselor, don't you want to put that -- your question in context? Why wouldn't you want to do that?

Q. I want to ask you the questions I want to ask for the reasons I want to ask them, and your lawyers can ask you whatever questions they want to ask. That's how the process works. And so I want to ask you just the questions I want to ask you, Doctor DiMarco, and we'll let whoever decides these issues make whatever use they want of them, and --

A. Just, please, understand I'm a teacher by

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nature.

Q. I understand. And I'm not --

A. Taught most of my life --

Q. I understand.

A. -- and I love to put things in contexts.

Q. I understand. Well, let me just ask you the questions.

It's true, isn't it, that after the Research Department developed an innovation that it was passed on to marketing for use in products if it was appropriate. Am I right about that?

A. Yes, you are.

Q. Now. Do you recall a Doctor Adolkofer?

A. Say the name again.

Q. Adolkofer.

A. Adolkofer?

Q. Yeah.

A. Yeah.

Q. Who was he?

A. He was a -- part of an international or European group, I think.

Q. Was he associated with the R.J.R. Tobacco Company in some way that you recall?

A. Now, let me --

Q. I'll show you documents, if you recall this.

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A. Doctor Adolkofer headed a group in Europe of tobacco companies. That's what he did, and we were a part of the group, I suspect.

(Plaintiff's Exhibit 13 was marked for identification.)

THE WITNESS: Now I tried -- it won't stay.

MR. HALL: The sticker stamp fell off.

THE WITNESS: Do you have another one? It lost its stickiness. I got it.

MR. MCCLAIN: That's better.

THE WITNESS: Thank you.

MR. MARPLE: Is this 13?

COURT REPORTER: Yeah.

MR. MARPLE: Let me state for the record that the court has rules on Exhibit 13 in *Burton* overruling claim of privilege. Reynolds continues to insert its privileges.

A. May I ask, do we know who wrote this?

Q. BY MR. MCCLAIN: I was hoping you'd tell me.

A. Well, of course, you know --

Q. We can look at -- we can look at a log. Maybe counsel can supply it. Do you recall from the log who wrote it?

MR. MARPLE: I do not have that information. I mean, it's obviously been out in the case.

MR. MCCLAIN: Do you have the log?

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MR. MARPLE: We did give you a log.

MR. MCCLAIN: Does Mary Jo have it? Do you have the log?

MS. MIDDELHOFF: I'm sorry, Ken, I don't.

MR. MCCLAIN: Okay.

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MR. DAVIS: Just -- Bob, just -- just wait for his questions, Bob.

Q. BY MR. MCCLAIN: Do you know that ---

Who is Mr. Tucker? Charles Tucker?

A. My memory serves me right, Charles Tucker, was in the Marketing Department, but not for long during my

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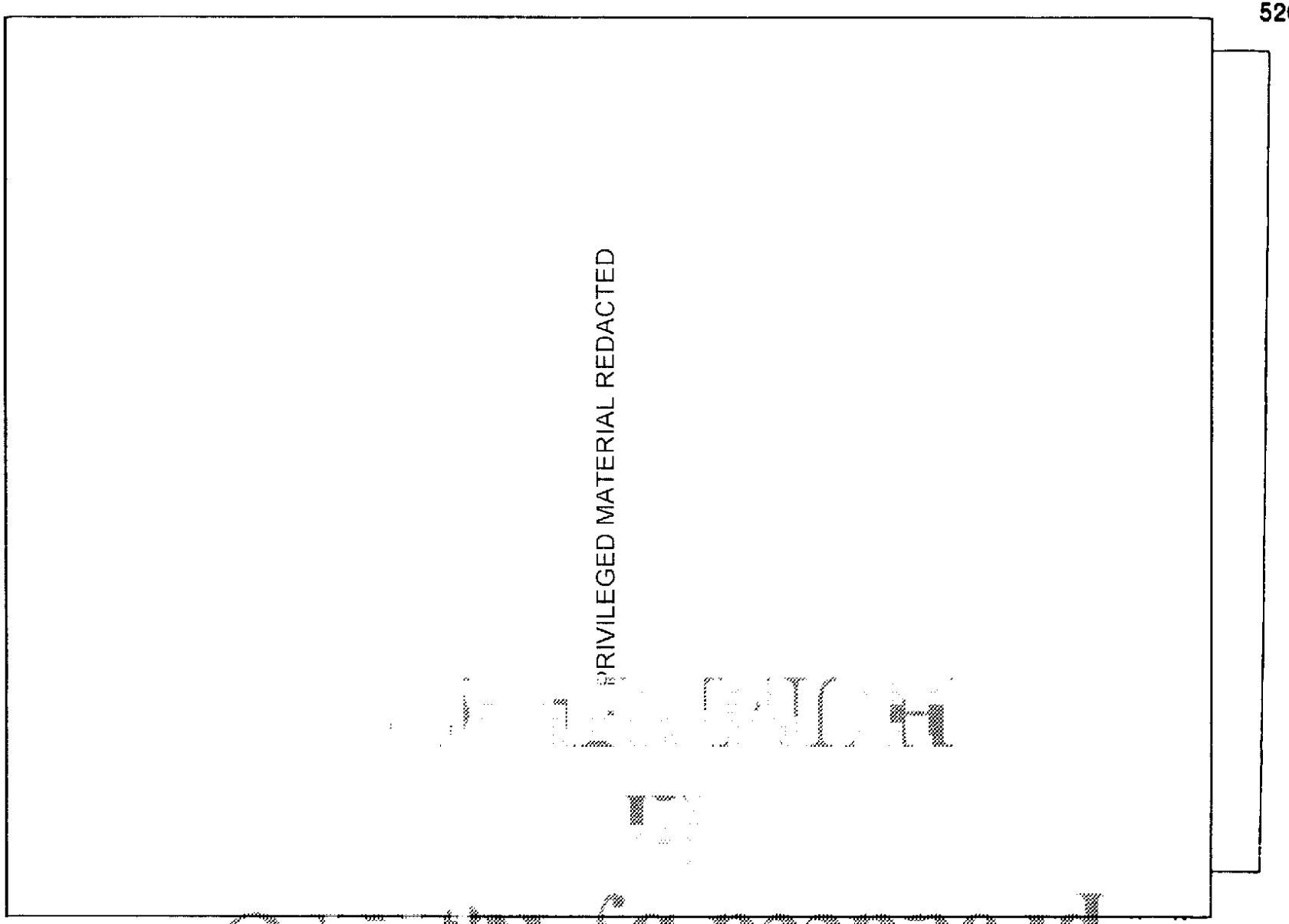

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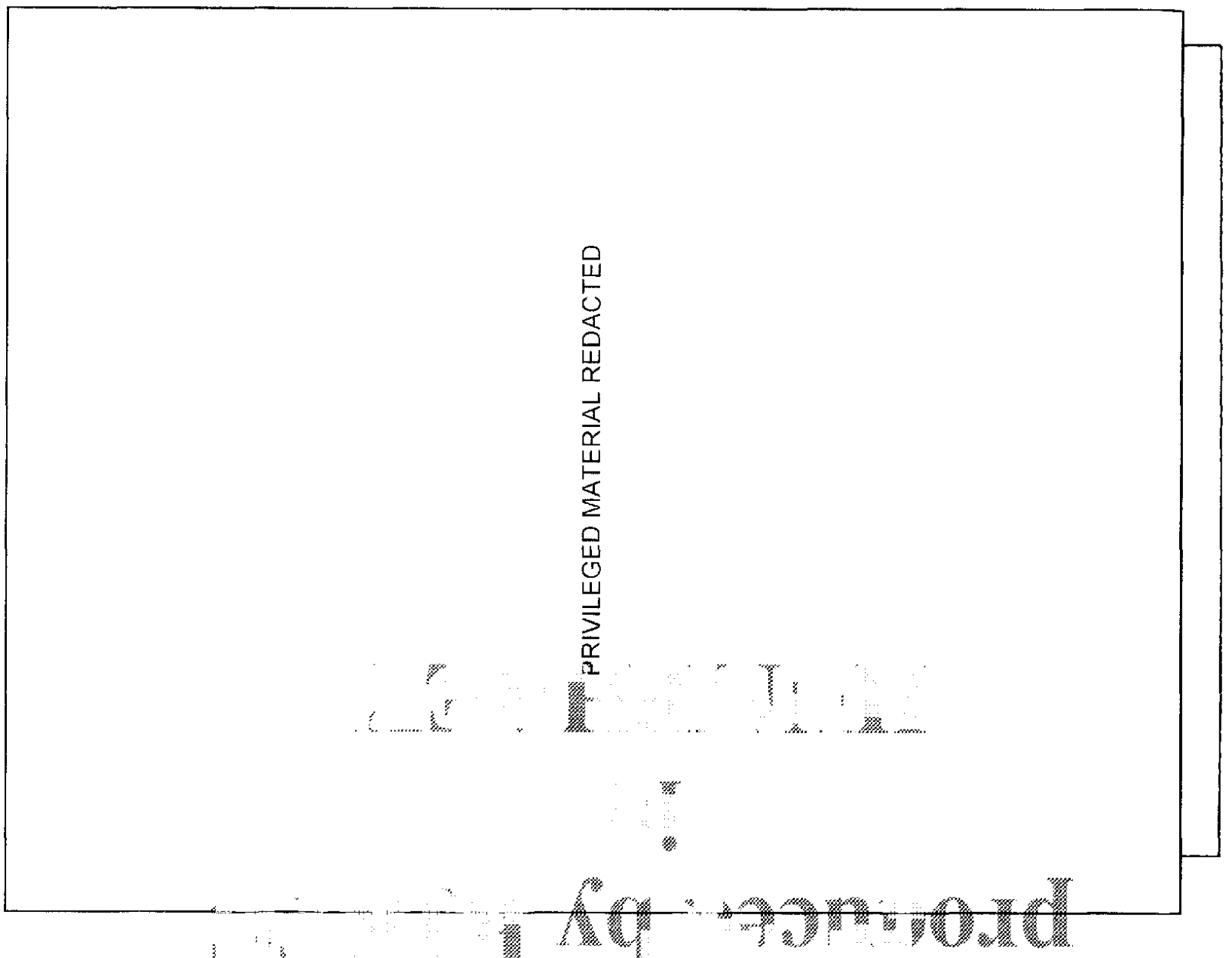

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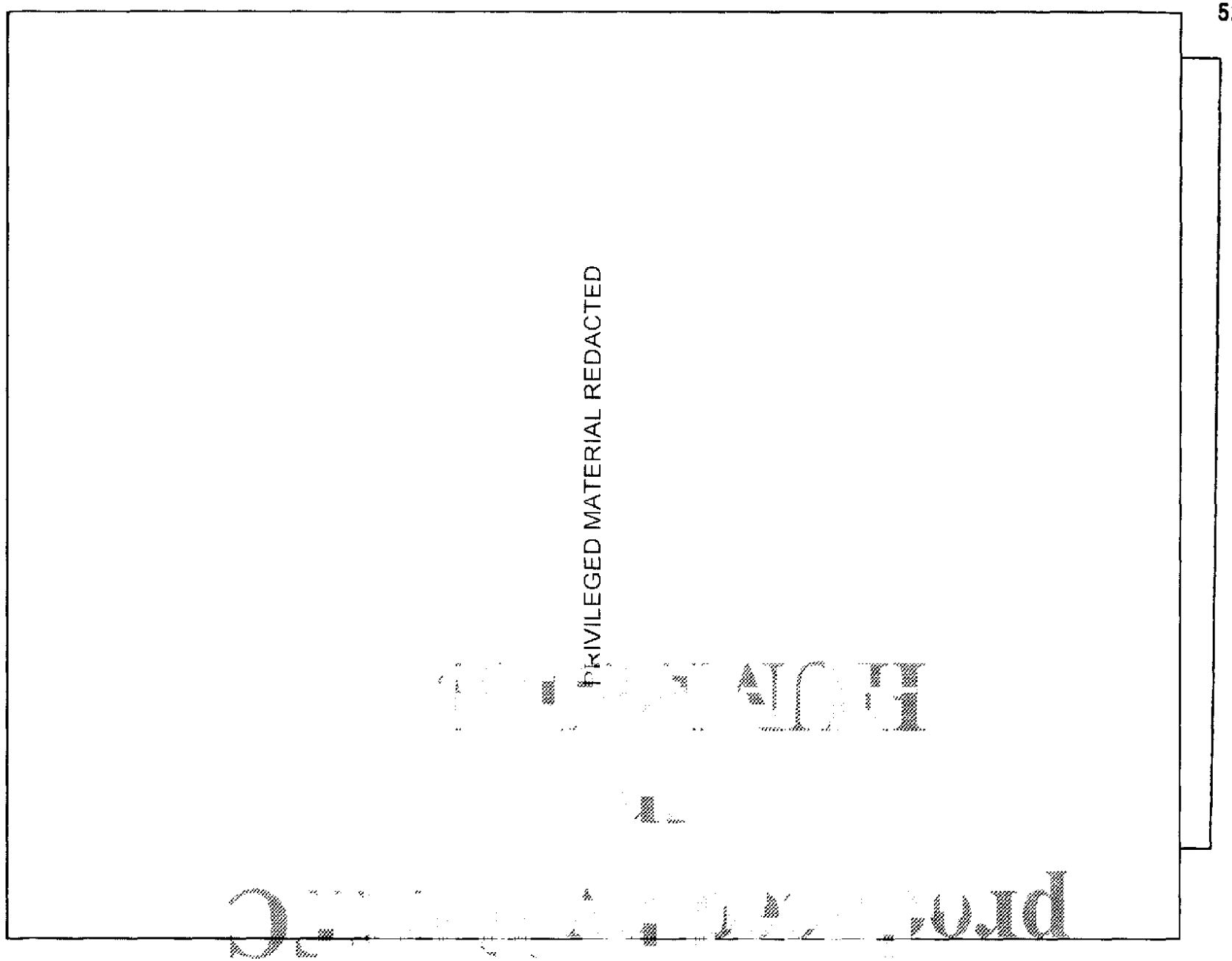

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Q. Do you know anything, Doctor DiMarco, about a so-called gentlemen's agreement among the tobacco companies not to do biological research in-house?

A. I certainly did a lot of it.

Q. Who was Frank Colby?

A. Frank Colby was -- I think I'd classify him as a librarian.

Q. And who is Mr. J. Giles?

A. He certainly worked for the company. If you ask me what -- more specifically what he did -- remember I had about eight hundred (800) people working for me at one time, but his name certainly rings a bell in R&D.

Q. Let me show you Exhibit --

(Plaintiff's Exhibit 20 was marked for identification.)

MR. MARPLE: Give us a just a moment to see if

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there's any privilege claim on that.

MR. MCCLAIN: It's been overruled.

MR. MARPLE: It has.

MR. MCCLAIN: It's *Burton* Exhibit 37.

MS. MIDDELHOFF: No, it's not privileged.

MR. MARPLE: We're not asserting any privilege on it. It may -- it's probably on your list and it's one that we didn't object to on privilege grounds.

Q. BY MR. MCCLAIN: This is from Mr. Colby who's identified as the Associate Director of Scientific Issues in the Research Department. Is that his title?

A. I have no idea. I thought of him as the librarian, because he was the head librarian as I remember.

Q. And Mr. ---

He's writing this to Mr. Giles and he says, "Information was obtained that Philip Morris U.S.A. doesn't live up to the alleged, quote, gentlemen's agreement of not having animal laboratory facilities on their premises in this country."

Do you see where I read that?

A. Uh-huh.

Q. Had you been informed about this gentlemen's agreement not to do laboratory research on your premises?

A. I don't know that there was an agreement. I can tell you that we had an animal facility and we used it

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extensively.

Q. All right. And do you know --

A. I've not seen this document, by the way. It occurred -- I mean, it was written certainly before my tenure.

Q. You were there about a year after this.

A. Yes.

Q. Do you know whether or not Reynolds developed the animal laboratory in response to Philip Morris not living up to the agreement not to do this research?

A. No. I do know that the laboratory was developed at the request of my department. We needed it and we built it. An up-to-date one, by the way. It met all the requirements of all the associated government agencies.

Q. Now, going back to the previous document, during the time that you were advocating doing research to investigate the alleged tobacco disease links, did anyone mention to you this gentlemen's agreement that existed between tobacco companies not to do biological research on-site?

A. I don't recall that, no.

Q. Now, in this document back to the September 27, 1982, it quotes you as advocating that you should be putting out article -- an article a month telling about the benefits of smoking. Is that right?

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MR. MARPLE: Let me object to that question on the grounds of attorney/client privilege and attorney work product.

MR. MCCLAIN: How -- how in the world could it be? It said Witt left the meeting, DiMarco and Morse mention the series of meetings they were having with Ed Jacob, and that they mentioned -- then it quotes DiMarco as saying in a meeting with our lawyers that "we should be putting out an article a month telling about the benefits of smoking to the president of the company." How in the world can that ever be privileged?

MR. MARPLE: If you want to ask him about that statement, if he made that other than the context of the conversation with lawyers.

MR. MCCLAIN: That's what I'll ask.

MR. MARPLE: I have no problem with that.

Q. BY MR. MCCLAIN: Tell me --

A. Where are we, by the way?

Q. I'm here on this statement that --

A. But what document, though? I'm still on the --

Q. That's it.

A. Oh, I didn't see that.

Q. Page 2. It's the -- one, two, three, four, five -- fifth paragraph down, and it says, "DiMarco said we

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should be putting out an article a month telling about the benefits of smoking."

Do you see that?

A. No, I haven't found it yet.

Q. It's the paragraph beginning with, "After Witt left."

A. No. If you want to talk about the kind of problems that we did have, when you talk about the parking problem referred to here, that's the tough one.

Q. I have a different problem, though. I've got a client without legs. That's the problem that I'm addressing. The paragraph --

A. I still don't see it.

Q. "After Witt left." Do you see that?

A. Yeah.

Q. Okay. It's the last sentence. "DiMarco said we should be putting out an article a month telling about the benefits of smoking."

Do you see that?

MR. MARPLE: Wait a minute. I've got to object to that question.

A. You said the paragraph after that --

MR. MARPLE: It's calling for attorney/client privilege and work product information and --

Q. BY MR. MCCLAIN: Well -- well, I ---

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Doctor DiMarco, do you see where that refers?

MR. MARPLE: Let me -- I've got to object to that question on the same grounds. You're asking him about privileged information in a document for which we're claiming privilege, and there's been no ruling otherwise by the court.

MR. MCCLAIN: I --

MR. MARPLE: If you want to ask the question I think you want to ask, I may not have a problem with that.

MR. MCCLAIN: Okay.

Q. BY MR. MCCLAIN: Doctor DiMarco, do you ever remember advocating that Reynolds should be publishing an article a month telling the public about the benefits of smoking?

A. I don't remember that specifically. First of all, an article a month is pretty unrealistic in any terms, but I did advocate that we do research on the benefits of smoking.

Q. All right, now.

A. And we did.

Q. Doctor -- yes. Did ---

You mentioned that Reynolds published -- what did you say, sixty (60) papers? Is that what you said?

A. On average.

Q. A year?

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A. On average.

Q. All right. Sixty (60) papers a year. Did -- can you cite me to any paper that was published by Reynolds which concluded that smoking was a cause or risk factor of disease in humans during your tenure?

A. Let me be sure I understand your question. Would you repeat it?

Q. Yeah. Do you recall publishing a paper during your tenure as the company's chief scientist that concluded that smoking was a risk factor for cancer?

Q. We only published in referee journals where you must have data to prove whatever you're publishing, and we had no data to prove that at all.

Q. So the answer is no?

A. The answer to that question is no, and the reason why. I'll try to speak up for you.

Q. Did you ever publish an article which concluded that cigarette smoking was addictive to humans?

A. We published lots of articles about what we researched on addiction. I don't think any of them ever said tobacco was addictive unless you define the word "addictive."

Q. So the answer is no.

A. Under the -- what the -- under the context that I presented it, yes.

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Q. Did the R.J. Reynolds Company, during your term as the company's chief scientist --

A. Not chief scientist. Director of Research.

Q. Let me restate it. Doctor DiMarco, in your tenure as Director of Research, did the company ever publish an article which stated that cigarette smoking could cause heart disease or circulatory disease or any diseases to humans?

A. Again, we were not equipped to do that kind of research. Although the company paid for a lot of that kind of research, we were not equipped to do that in-house, and we wouldn't publish anything we didn't do in-house, obviously.

Q. Do you recall any article that was funded by Reynolds which concluded that tobacco was the cause of any disease or was addictive to humans that you can cite me to?

A. Not that I could cite you to. You're asking for recollection, obviously?

Q. Yes, sir. Now, I want to turn to the issue of nicotine if we can. And this is a memo from Mr. Teague.

(Plaintiff's Exhibit 21 was marked for identification.)

Q. BY MR. MCCLAIN: This document is not dated on its cover, Doctor DiMarco, but there are documents which are attached which date it to 1973, if you'll look at the

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back.

Did you, at the time that you began research on the role of nicotine and its relationship to smoking, review the work that had been done previously by the Research Department?

A. I personally? What I worked on previously in the Research Department would make a pile higher than this building. No, I did not.

Q. Let me ask you if you were aware from your discussions with ---

Turn to Page 2. This is from Doctor Teague --

A. To who? Certainly not me.

Q. No. You weren't there at the time. This is a memo prepared by Teague in which Doctor Senkus indicated in his deposition what was prepared routinely within the Research Department by Doctor Teague to generate discussion and research, just for backup. That's my representation to you, but that's in essence what he told us about this document.

My question to you is in regard to Page 2. It says, "In essence, a cigarette is a system for delivery of nicotine to the smoker in an attractive, useful form. At normal smoke pH, at or below about 6.0 essentially all of the smoke nicotine is chemically combined with acidic

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substances, hence is non-volatile and relatively slowly absorbed by the smoker. As the smoke pH increases above about 6.0, an increasing proportion of the total smoke nicotine occurs in free form, which is volatile, rapidly absorbed by the smoker, and believed to be instantly perceived as nicotine, quote, unquote, 'kick.' Chart VIII shows how proportion of free nicotine increases as pH goes higher."

Let me just stop for a moment.

Did you have discussions with people in the Research Department of the subjects of quote, unquote, "nicotine kick and free nicotine" before beginning your research on nicotine?

A. You're qualifying that before doing our research on nicotine. I don't recall that, no.

Q. What about after your research on nicotine?

A. I don't recall that either. You're asking me specifically when I had these -- might have had these discussions.

Q. Do you recall ever having these discussions?

A. We've always talked about nicotine. We sell a lot of nicotine. Why would we?

Q. All right. The --

A. That doesn't mean I agree with what's in this document. I don't agree with it.

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Q. Look down at the third paragraph, if you don't mind.

A. You're going to force me to read the whole thing, if you're going to get very specific.

Q. Okay. If you want to. I'm trying to speed this up for you.

A. Because I really -- you know, this is -- this was told to you, it's a discussion piece. I suspect that's what it was.

Q. Well, I think that that's a fair characterization. He was trying to summarize his state of understanding of nicotine and the role that it played in the advance of Marlboro brands versus -- versus Winston and other cigarettes manufactured by R.J.R. I think that was the context of this document, but you can review the whole thing if you want.

A. Well, I don't know if I have to, unless you're going to force me to.

Q. Well, I want --

A. Did he also tell you we've had a lot of discussions over the years about nicotine? We as a company took nicotine out of the product. We never added it.

Q. Well, we're going to talk about that because there's some issue here regarding some smoke chemistry that I want to address with you if I can. It says, "As a result

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of its higher smoke pH, the current Marlboro, despite a two-thirds reduction in smoke, quote, unquote, 'tar' and nicotine over the years, calculates to have essentially the same amount of, quote, unquote, 'free' nicotine in its smoke as did the early Winston."

A. So --

Q. Did someone discuss that subject with you?

A. I don't recall if they did.

Q. Is that consistent with your statement that the amount of nicotine has declined over the years?

A. No. I didn't say it's declined. I said we took it out of our products.

Q. Okay.

A. We had a plant that did nothing but that.

Q. Okay. It states here -- it states here that the amount of free nicotine in its smoke has been about the same even with a reduction of nicotine from the cigarette itself. Is that true?

A. I don't know.

MR. MARPLE: Objection.

A. I mean, I don't remember. How could I remember?

Q. BY MR. MCCLAIN: You don't remember. All right. You don't have any quarrel with this statement, however.

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MR. MARPLE: Let me object. This is before he was at the company. And also my understanding of the purpose of these depositions were to ask him about exhibits on your exhibit list that the court had made some rulings on privilege and it certainly is falling outside of that, so I object on that basis the questioning about this document.

Q. BY MR. MCCLAIN: Did you have some quarrel with this statement as being a true statement?

A. Which statement are we talking about?

MR. MARPLE: Objection.

Q. BY MR. MCCLAIN: The statement that the -- that even though there's been a two-thirds reduction in smoke 'tar' and nicotine over the years, that the amount of free nicotine was about the same as --

A. I have no reason to know one way or the other.

Q. Okay. It says, "Over the same period, with some reduction in smoke pH and about two-thirds reduction in smoke 'tar' and nicotine, the calculated amount of free nicotine in Winston smoke has decreased by two-thirds. Thus currently the calculated amount of free nicotine in Marlboro smoke is almost three times the amount in Winston smoke."

When you came aboard, was that something that you were asked to address, the difference between free nicotine and Marlboro versus Winstons?

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A. No. We knew as scientists that the pH affected the delivery of nicotine verses pre-nicotine, that is. Of course.

Q. So --

A. We don't -- why would we ---

Why would I be interested in that?

Q. I -- why was Doctor Teague? I don't know.

A. I don't know. Doctor Teague, by the way, is a very bright guy who can -- who, as I remembered it, I liked him. I told you I couldn't remember exactly what he did, but he loved to -- he could start a discussion on anything, including religion. Certainly you can see what he did here.

Q. Yes.

A. I mean, he could start all kinds of discussions. He just enjoyed it. He loved it.

Q. Was he a confident scientist?

A. I think Doctor Teague was a bright -- bright guy. I don't -- can't think of a good piece of research that he's ever done. But, again, that's been a long time ago. He left the company during my tenure, but, I think, in the early part of my tenure. I just can't think of a hands-on piece of research that he's done where I can answer that question competently.

Q. All right.

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A. I just can't.

Q. Because you didn't have a relationship with him?

A. No, I had a relationship with him. I just can't remember him doing that.

Q. All right.

A. And to answer that question, I'd have to remember that.

Q. All right. So you can't answer the question. The -- look down here. It says here on Page 3 -- it says that "These differences in nicotine impact" -- this is on Page 3 of the document under heading V. second paragraph.

"These differences in nicotine impact and other smoke qualities arising from smoke pH increases would be expected to give rise to differences in consumer response, hence market performance."

Did you study that issue when you were Director of Research, Doctor DiMarco?

A. I'm rereading the sentence. (Reviewing document.)

Q. Okay.

A. I don't recall studying that at all. I can tell you that, as I recall it, the market position of Reynolds products in those days -- this is long before I joined the company -- they had a better market position than

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Philip Morris, so I don't know why we'd be interested in doing what they do. I don't -- I mean, I just can't think of one.

Q. Well, by the time you became Marketing Director of Philip Morris and --

A. Huh-uh. I've been accused of lots of things, but never that.

Q. Let me start again. Doctor DiMarco, when you became Director of Research in 1982, Philip Morris and Reynolds were in a virtual dead heat in terms of market share. Isn't that true?

A. No, I think we owned the market share.

Q. In '82 you did?

A. I think we did, yeah.

Q. Ultimately, did Philip Morris exceed your market share?

A. Yes, they did.

Q. And was one of the issues that you were asked to address was the ability of your products to deliver free nicotine?

A. No. The understanding -- my understanding at the time was the reason they surpassed Reynolds was because of their cowboy. We didn't have a cowboy.

I was asked as a Research Director, could we reproduce one of their products. The answer was we probably

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could, but why would we? Why should we? In a sense we had our own product that was doing very well in the marketplace. Why would you want to reproduce theirs? And, by the way, this is a pretty strong position with me.

Q. The -- was the issue that you were asked to reproduce the same amount of free nicotine in the cigarette?

A. I have no idea, but I suspect that Marketing would like to have tested it to see what the differences might be in acceptance. And that's all they could do, by the way.

Q. And -- and, but --

A. You keep coming back to free nicotine, and I kept telling you that never motivated me that I can recall.

Q. Well, I'm just looking at this document that was -- that --

A. It was written ten (10) years before I got to the company, and you said written for discussion purposes. You said it. I didn't say it.

Q. Yes, I did.

A. It's -- and I told you, as I remember Claude, he could do that very well. He could start a discussion on anything.

Q. Well, isn't that a valuable function in the Research Department?

A. You better believe it.

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Q. That's -- that's the place where --

A. You better believe it.

Q. -- lots of good research begins, doesn't it? That's what --

A. And there's no lack of it in research.

Q. That's what researchers have to do.

A. Precisely.

Q. All right. Now. One of the ways of adjusting the pH of cigarettes and hence, impacting nicotine deliveries is the pH of the smoke. Am I right?

A. Uh-huh. With -- with limitations, by the way. Primary limitation is, as I remember it, harshness.

Q. All right.

A. And in the end that's -- you couldn't -- I could never understand the argument with nicotine because if you -- if you formed a lot of free nicotine, you couldn't smoke the product. You just couldn't. It was just too harsh. And that's one of the reasons we used a tobacco called burley tobacco that naturally had a high pH. We took a lot of the burley tobacco out because we didn't want tobacco to be harsh.

Q. Let me ask you --

A. As I recall it, by the way.

Q. Did ammonia increase smoke pH?

A. Ammonia under certain circumstances can, yes.

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Q. And let me hand you a document that we'll mark as Exhibit --

MR. MCCLAIN: Which one is this?

MR. HALL: Twenty-two.

(Plaintiff's Exhibit 22 was marked for identification.)

Q. BY MR. MCCLAIN: Do you know who produced this document and when?

A. Well, the lawyers produced it to us. That's all I can tell you.

Q. That doesn't help me a bit.

A. No. I don't know who wrote it. Or when.

Q. Or when. However, from its internal documents, it's sometime after 1979, because there's a reference in the internal page of 1979.

It talks about the technology, ammoniation, the definition as being "The reaction of ammonia with tobacco to produce ammoniated tobaccos which smoke differently and produce a milder smoother flavored smoke."

Is that your understanding of what ammoniation is?

A. No. No. As I remember -- you know, you've got to remember, I'm not an expert in this area. Is -- ammoniation increases the pH and produces a harsher product. You would expect -- at least I would expect ammonia to do

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that.

Q. It says, "R.J.R. introduced ammoniated sheet material in the Camel filter product in 1974." Do you see where I am?

A. Uh-huh.

Q. "Better market performance was indicated in the subsequent years." Was that true as far as you understood it?

A. I have no idea.

Q. "Low 'tar' products at R.J.R. were designed with ammoniated sheet material beginning in '74. R.S.M. studies showed that" -- is that Reynolds? What is R.S.M.?

A. It must be research studies of some kind.

Q. "R.S.M. studies showed that ammoniation was one of the major consumer recognized product attributes tested. Ammoniated sheet was introduced into the Winston K.S. product in 1979. Market tests indicated significant product improvement. Recent internal panel testing of products with ammoniated flue-cured tobacco have shown consistent and significant product improvement."

And then it lists the products characteristics: "Higher smoke pH," is one listed. And then skipping down. "Cleaner taste with more free nicotine." And then, "Stronger physiological impact with less harshness."

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Were these the things that you were asked to study?

A. This was done, I suspect, long before I got there. And it's the reverse of what I would expect in my limited knowledge of these matters. But I have no reason to disagree with what's written here or agree.

MR. MCCLAIN: Let's take a break for a minute. I need to go to the rest room.

VIDEOGRAPHER: We are off the record at 2:15.

(Off the record)

(Back on the record)

VIDEOGRAPHER: On the record at 2:19.

Q. BY MR. MCCLAIN: You were there 6/9/82, right?

A. I think I was, yes.

Q. Let me show you an exhibit on ammonia.

(Plaintiff's Exhibit 23 was marked for identification.)

A. (Reviewing document.)

Q. BY MR. MCCLAIN: And if you look back within the document, it appears they're out of order, but it appears to be the cover letter to you from Mr. Bernasek and Mr. C.W. Nystrom on these subjects.

A. Doctor Golberg, by the way, just for your information, was an outside consultant for me. A world-

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famous toxicologist who's published lots of books, and has also been president of a very large toxicological firm. Heck of a guy.

Q. Did he -- did he warn you about the effects of nicotine on the human system?

A. What do you mean by that?

Q. Did he tell you that nicotine could cause vascular constriction in people that used it?

A. Just the reverse.

Q. Huh?

A. Just the reverse. Nicotine is a -- or cigarettes in general is a dilator, not a constrictor.

Q. Did he mention to you the fact that people who smoked and consume nicotine could get peripheral vascular disease, as an example?

A. I don't see data that would indicate that at all. In fact, most of the data that I've seen and is published in the government documents say that people who smoke have lower blood pressure than people who don't smoke. Again, because nicotine or cigarette smoke, in general, is a dilator, not a constrictor.

Q. Okay. And have they pointed out to you that in some people that can cause there to be a lack of circulation to the limbs?

A. I've never seen data to that effect.

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Q. Do you know what peripheral vascular disease is?

A. I think I do.

Q. Do you know that it is a condition which causes individuals to end up ultimately losing their limbs?

A. I suspect -- I don't know that, but I could see why it would.

Q. And do you have some understanding that that is caused by smoking?

A. No. I never saw any data that said that -- any data that said it caused it, I should say.

MR. MCCLAIN: Let's mark this exhibit.

(Plaintiff's Exhibit 24 was marked for identification.)

MR. MCCLAIN: Do you have any privilege claim as to this document?

MR. MARPLE: I don't think so.

MR. MCCLAIN: Okay.

Q. BY MR. MCCLAIN: I want to -- I'm only bringing this document to your attention because your mention -- mentioning your work with a toxicologist.

Did you ever see this document, "The Health Consequences of Smoking: Cardiovascular Disease, a report of the Surgeon General"?

A. I might have.

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Q. Would you look at Page Roman Numeral VI. It's down in the left-hand corner you can -- under other cardiovascular disease?

A. I'm -- I'm just looking over, as I usually do, who the authors were.

Q. All right.

A. I don't have Page 6. I don't think I have Page 6. I have a 5 and a 7.

Q. It's 5, and if you turn over here that's Page 6, that's Page 7.

A. Oh. All right.

Q. Okay. You see where, "Other cardiovascular disease"?

A. Uh-huh.

Q. Can you read that paragraph?

A. I'll read it. (Reviewing document.) Yes, I read it.

Q. Do you see that it says, "Peripheral vascular disease is caused by smoking"?

MR. MARPLE: Objection.

A. No, no. There's reference to etiological data. It doesn't say anything about causing.

Q. BY MR. MCCLAIN: It says, "Cigarette smoking contributes to the development of aortic atherosclerosis and atherosclerotic [sic] peripheral vascular disease" --

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MR. MARPLE: Objection.

Q. BY MR. MCCLAIN: -- "(A.P.V.D.)"

MR. MARPLE: I'm sorry. I'm just going to object. It says, "Arteriosclerotic peripheral vascular disease," not atherosclerotic.

Q. BY MR. MCCLAIN: Why don't you read it to us?

A. No. I'm not going to read it to you. I can hardly see it.

Q. Arteriocardio vascular -- let's start again.

A. I'm in the process of getting --

Q. Do you see ---

Doctor -- Doctor DiMarco, do you see where it says that "Cigarette smoking contributes to the smoking of aortic"

A. Athero--

Q. -- "atherosclerosis and arteriosclerotic peripheral disease (A.P.V.D.)"? Do you see that?

A. Uh-huh.

Q. "Ninety percent of patients with A.P.V.D. are cigarette smokers, and the successful management of this disease includes complete smoking cessation by such patients."

A. I read that.

Q. Did your -- did your world-famous toxicologist ever talk to you about that?

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A. I don't know that I asked him the question.
Q. Is the answer you don't recall?
A. No. I said that I don't know that I asked him the question.
Q. So you do recall not asking him about it?
A. No. I said I don't remember asking him the question.
Q. Okay.
A. I'm just trying to point out to you that we had a lot of outside really famous people directing the -- not directing, but helping us in forming our research program. Because you keep insisting that the lawyers have and saying, no, they haven't.
Q. Well, you know, the fact that -- the fact that I can call the president on the phone is irrelevant to the issue. What did he tell you? Did he tell you that cigarette smoking caused disease or not?
A. I didn't ask him the question --
MR. MARPLE: Let me object to the question.
Q. BY MR. MCCLAIN: Why not?
MR. DAVIS: Objection.
MR. MARPLE: It's argumentive to -- both times it's argumentive.
Q. BY MR. MCCLAIN: Why not? Why didn't you ask him the question if he was a world-renowned toxicologist,

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whether cigarette smoking caused disease?

THE WITNESS: Can I answer?

MR. DAVIS: Sure.

A. I might have, by the way, but I think the answer would have been exactly what mine is. You know, there has never been -- do you want me to repeat this -- mechanistic proof that cigarettes cause cancer in humans along with many other things. But we always acted as if -- because you could not ignore the data, the statistical data, as if it did -- always.

Q. BY MR. MCCLAIN: When was this conveyed to the public? Do you know?

A. I've said it many times in many speeches.

Q. Do you ever recall an advertisement for R.J.R --

A. No. I don't.

Q. -- an R.J.R. product, which says that "we assume cigarettes will cause disease in humans"?

A. I didn't say that. Did I say that?

Q. I thought you did.

A. No, I didn't. I said we did not ignore the statistics. Although statistics cannot cause, you know, that cannot prove causality, but we did not ignore the statistics. And even -- and the statistics said, "hey, pay attention -- pay attention to this." And so we acted as if

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it did, even though it was not proven to a good scientist mechanistically. That was the semantics, by the way, we were referring to before between the lawyers and I.

Q. What -- what effort did the Reynolds Tobacco Company take to educate the public about this important health concept? Did it take any that you're aware of?

A. What concept?

Q. The concept that statistics can't prove causation, but you should assume that it does cause disease.

A. I didn't say that. I didn't say that at all.

Q. Well, I guess that's why it's confusing to people what Reynolds' position on this subject is.

A. I told you what my position has always been, and that Reynolds accepted it and allowed me to act that way, as did the Director of Research.

Q. Look back at that document about, "Can we speak frankly about cigarette smoking." Do you remember that document that we had in the beginning?

A. No, I don't.

Q. This is the document. It's Exhibit 7. "Can we have an open debate about smoking."

A. Yeah. Well, what do you want to --

Q. Well, the question I have is, where in this document do you convey to smokers --

A. I didn't -- not me. You're talking about me?

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Q. The company.
A. No. I didn't write this.
Q. I know. Where does the company --
A. I have no idea where it might be.
Q. -- convey what the Research Department knew?
A. What did we know?
Q. That you couldn't ignore the statistics.
A. The company acted that way.
Q. How?
A. How? By allowing us to do the kinds of things that --
THE WITNESS: May I?
MR. DAVIS: Sure.
A. You read in one of those records that I recommended that F.D.A. -- we be controlled by F.D.A. Do you know why? I did a lot of work with F.D.A. before I joined the company. I had that responsibility at a very good food company. And I saw nothing that we were doing, nothing that we were doing that would give the F.D.A. concern. Nothing. That's why I recommended it.
Q. BY MR. MCCLAIN: And do you know the company as of last year was still challenging the F.D.A. jurisdiction and were successful in overturning the F.D.A. jurisdiction over cigarette smoking?
A. I have -- what happened last year, I have no

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idea.

Q. So --

A. You had -- you saw that I was recommending -- I told you why I was recommending it. I recommended it because we were doing nothing that would give F.D.A. concern.

Q. Doctor DiMarco, what effort, that you're aware of, was made to convey to the smoking public what you and research knew about smoking and health? Anything that you're aware of?

A. Now, what we -- by what we knew --

MR. MARPLE: Objection.

A. -- do you mean what?

Q. BY MR. MCCLAIN: All of the things --

A. That we were paying attention to the statistics?

Q. Yes.

A. Yeah. I have -- that was not my job, by the way. I have said it at many, many public occasions --

Q. I --

A. And it's probably on film, by the way.

Q. Well, I'll look for that. But the question I have -- the question I have is, are you aware of any public advertising or public information campaign?

A. I don't -- I would have no way of knowing one

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way or the other, I guess.

Q. Okay. Now. We got off on a little frolic and detour. Go back to this document on ammonia.

A. Which one now, 23?

Q. Yes. The 8/9/82 draft which, I think, the cover letter indicates was sent to you by Mr. Bernasek and Mr. Nystrom.

A. Bernasek, yeah.

Q. How did you say his name?

A. Bernasek. Edward.

Q. Bernasek. Okay. It says, "Attached are position papers describing our rationale for using the following additives in R.J.R.T. tobacco flavor formulations."

The first one is ammonia. And it says on the first page of the document of the draft, "Ammonia is used by R.J.R.T. in the following tobacco processing operations: (1) Denicotinization of burley tobacco," which you told us about, "and ammoniation of reconstituted tobacco."

Is that correct?

A. I don't see that it says ammoniation -- ammonia was used for denicotinization, but we did denic products, yes.

Q. Ammonia -- do you see that up at the top of the page where I'm referring?

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A. Denicotinization of tobacco.

Q. Of burley tobacco, and ammoniation of reconstituted tobacco. Do you see that?

A. Yes. No, you indicated -- I thought you said that we used ammonia to denicotinize? No. I don't think we did. We might have, but I don't think --

Q. It says, "Ammonia is used by R.J.R.T. in the following tobacco processing operations: (1) Denicotinization of burley tobacco."

Did I read that accurately?

A. Yes, you did.

Q. All right. And "(2) Ammoniation of reconstituted tobacco." Was that accurate?

A. I don't know. It has to be. It comes from very competent people. I suspect it's accurate, yeah.

Q. Is it true that -- that the ammonia that was removed from nicotine tobacco was added back to reconstituted tobacco sheet?

A. "Is it true" -- ask the question again.

Q. Is it true that the nicotine that was removed from burley tobacco was added to the tobacco sheet?

A. Some of it was added to the tobacco sheet. There's no question about it. Net -- net -- we had loss of tobacco. I mean, loss of nicotine.

Q. Let's -- let's talk about that in just a

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minute. But it's true, is it not, that the nicotine is taken out of the tobacco in processing, so-called, tobacco sheet, right?

A. No. Sheet was made from material that did not have nicotine.

Q. All right. And cigarettes are made from the tobacco ---

Describe the process if you can. What is tobacco sheet, can you in layman's terms?

A. A tobacco sheet is a process, as I remember it -- and I was never an expert at that either -- where, in fact, you produce a tobacco-like material to reduce the -- primarily to reduce the cost of tobacco, as well as to reduce the tar in tobacco. Because if people like lower tar cigarettes, one way to do that, and a good way to do, was to use a sheet.

Q. All right. In other words, these were other parts of the tobacco plants that were --

A. To manufacturing.

Q. -- manufactured like paper. Am I right?

A. It can be manufactured.

Q. That was made into pulp and then spread out into a long sheet, and to that -- to that nicotine had to be added, am I right, to make a cigarette?

A. We added nicotine.

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Q. You added. So it didn't have to be added?
A. No.
Q. All right.
A. And maybe in some cases it was not, according to how much -- what product you were selling.
Q. All right. That's a good point. Let's ask about that. It is possible to manufacture a cigarette without nicotine, is it not?
A. People have. Not successfully, but they have.
Q. Look over on Page 2 on this report that you received. "Ammoniation of Reconstituted Tobacco." It says, "Studies on the ammoniation of reconstituted tobacco" -- and I'm under "ammoniation of reconstituted sheet." It's kind of hard to read. They stamped something over the top.
A. I don't -- you're on --
Q. I'm on Page --
A. I'm on the table.
Q. I'm on Page 3.
A. Three. Oh, okay. I thought you said 2.
Q. Under "Ammoniation of reconstituted tobacco."
A. Uh-huh.
Q. "Studies of the ammoniation of reconstituted tobacco were started in 1973 as a result of R&D studies carried out during the fifties and early seventies. During

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the fifties, Doctor C.E. Teague, Jr., investigated the ammoniation of tobacco and tobacco stems and reported dramatic improvement in the smoking qualities of ammoniated tobacco stems. Smoke harshness and irritation were reduced and taste properties were improved."

"In the early seventies, a major R&D program was initiated to investigate the physical chemistry of tobacco and tobacco smoke in an attempt to gain a better understanding of factors affecting smoke harshness, irritation, and strength. These studies led to the following observations and conclusions."

"The pH of cigarette smoke is important to smoke quality and can be used as a measure of physiological strength of smoke -- of the physiological strength of smoke. And 2: Ammonia in smoke is one of the major pH controlling components."

All right. Was this ---

So do you now recall that you were aware of Doctor Teague's work --

A. No.

Q. -- when you began your work?

A. This didn't come from Doctor Teague.

Q. It identifies Doctor Teague's work in this memo that was prepared for you.

A. But this is a memo. I get twenty (20) of

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these a day.

Q. So you didn't read it?

A. I might have. I might not have. I probably read -- I -- look, you have to understand how a research operation runs. You hire competent people. I cannot, as a researcher -- I can't be expected, or can any other, by the way, to know the detail to everything going on in the company.

My modus operandi has been good to me my whole life as you hire very competent people in the fields that you need them and then they do the work. I mean, if I had to know everything, we'd be in an awful travesty. That would be true, I think, of any research operation. I trusted the people that I hired, and at the company, because I told you before we had very competent people at the company.

Q. So, Doctor DiMarco, so I'm clear, you have no recollection of reading this memo?

A. No, I don't. I don't know why I would. As I said, I get twenty (20) of them a day.

Q. I understood your answer, but as head of research it was your view that if you hired competent people, the head of research didn't have to read their memos?

A. No. I didn't say that at all. Most of the

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time, by the way, people send things to the head of research because, you know, you are the head of research. And if anything occurred that was important they'd call a meeting, and we would sit down and discuss whatever was important, which is often the case by -- that's how you spend your time.

Are we through with this now?

Q. Now, during this time period in the 1980's, the so-called low yield cigarettes were becoming a bigger part of your product line. Am I right?

A. I'm sure we were selling more. I don't know whether it was a bigger part. As a qualifier, I'm just not comfortable with it.

Q. Were you aware that your scientists were of the view that smokers of low yield cigarettes did not consume less nicotine?

MR. DAVIS: Objection.

A. I smoked low tar cigarettes, and I was certainly not aware that I wasn't getting less nicotine. In fact, I had to believe that I was getting less nicotine.

Q. BY MR. MCCLAIN: So even you didn't know that you weren't getting --

A. No, wait a minute. No, wait a minute. There's a self-regulator in tobacco. You cannot, you cannot exceed a ratio in general -- ten to one. So if you reduce

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the tar and try to increase the nicotine more than that ratio, you're going to be in trouble. And everyone knew that.

Q. Well, let me show you a document and see if I can get you to comment on it.

(Plaintiff's Exhibit 25 was marked for identification.)

Q. BY MR. MCCLAIN: This is to Doctor Alan Rodgman from J.H. Robinson. Are you familiar with those two gentlemen?

A. Of course I am.

Q. All right. Take time to read it.

A. (Reviewing document.) I read it.

Q. All right. First of all, is biobehavorial as referenced here one of your departments?

A. Yes, it was.

Q. And it says that Mr. Robertson is commenting to Doctor Rodgman that appeared -- which he comments is basically a sound scientific study.

A. Uh-huh. That's what they said.

Q. But it says, "The paper itself expresses what we in biobehavioral have felt for quite some time. That is, smokers smoke differently than the F.T.C. machine and may very well smoke to obtain a certain level of nicotine in their bloodstream." Did you see that?

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A. That's what they said, uh-huh.

Q. First, let me -- let's back up so that we have some understanding of what these terms are that we're talking about. There is a so-called F.T.C. method of measuring tar and nicotine. Is that not right?

A. Precisely.

Q. It's a machine that smokes cigarettes at a prescribed rate for a prescribed time and then measures what collected in a beaker, essentially. Am I right?

A. Right. When they fill the paper, that gets transferred to a beaker, yes.

Q. All right. And --

A. For the reason that you can now describe cigarettes in a very uniform manner.

Q. And those numbers are then reported to the cigarette smoker. Am I right?

A. They're reported to an agency of the government, who prescribed the method. The method -- I mean, the result of that are put on a pack of cigarettes.

Q. And you've also, as a low tar smoker, seen them also in advertisements. Am I right?

A. Sure.

Q. It says that "If a given level of nicotine in the blood is the final goal of a smoker, one would predict that he would smoke an F.F.T., full flavor tobacco, and

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U.L.T., ultra low tobacco, cigarette differently." Am I right? That's what it says?

A. Uh-huh.

Q. "If the smoker could obtain the same nicotine in his bloodstream from an F.F.T. and a U.L.T. cigarette by modifying his puffing/inhaling pattern, it would be expected that the blood cotinine level would be the same after smoking either cigarette on a regular basis. This all falls under the area of smoker compensation which we have been interested in studying for some time now."

Did you become familiar with this issue of smoking compensation?

A. Absolutely.

Q. And is it -- is it ---

Did, in fact, the Research Department do research on this subject?

A. You better believe it.

Q. It indicates at the bottom of this page that a study was done which showed -- in Germany, as between four different type of Camel and Marlboro cigarettes that regardless of whether they were ultra light or full flavor, the smoker got the same amount of nicotine in his blood.

Did you ever review that study?

A. I don't remember reviewing the study.

Q. Looking at the -- at an exhibit --

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A. But this, by the way, did spearhead some serious work on our part.

Q. Let me show you a draft of a document which is in the same time period but a couple months earlier.

(Plaintiff's Exhibit 26 was marked for identification)

Q. BY MR. MCCLAIN: I'm handing you Exhibit 26 which is a long document entitled "Smoker Compensation."

A. (Reviewing document.) I'm looking for who might have written the document.

Q. I don't have it. It's not identified within the document. It appears to be a review on this issue.

MR. MCCLAIN: Do you have the author?

MR. MARPLE: Does it show -- do we know who the author is?

MR. KREINER: It says Norman A.V.

MR. MARPLE: To whom? Does it say to whom?

MR. KREINER: Recipient Sam Witt.

MR. MARPLE: Reynolds -- this is not -- this is a privilege -- a document for which Reynolds is claiming privilege attorney/client and work product, attorney work product. And this is not one you have submitted to the court for a ruling.

MR. MCCLAIN: This is -- this is *Burton* Exhibit 67.

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MR. MARPLE: All right. Thanks. We'll check it and see. I apologize. This is one in which the court overruled our claim of privilege.

MR. MCCLAIN: Right.

MR. MARPLE: Sorry. We continue -- Reynolds continues to assert its objection -- privilege objection to this document.

Q. BY MR. MCCLAIN: Did you know Mr. Norman?

A. I don't know that I do. I don't recall the name at all. Is he at -- was he an employee of ours? I don't remember his name.

Q. Let's look at the document, the content, and see if you can tell us about these subjects. "Smoker compensation review. With the advent of lowered tar and nicotine delivery cigarettes, the notion developed that people modify their smoking habits depending upon the type or delivery of the product smoked. This notion is often termed smoker compensation or compensatory smoking behavior. A body of research has been performed in which various aspects of the compensation phenomenon have been studied. This review is not intended to be an exhaustive survey of the scientific literature. Rather, it is a review of the types of behaviors people might use to compensate, ways in which the behaviors have been measured and the impact of the behaviors on cigarette delivery ranking schemes."

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Do you have an understanding of the term, "smoker compensation" and/or "compensatory smoking behavior"?

A. Yes, I do.

Q. Can you describe what that concept is?

A. Just what that says.

Q. So this is an accurate description as you understand it?

A. People might smoke a low tar cigarette differently than they smoke a high tar cigarette.

Q. All right.

A. Now, at the time I don't remember that we were doing an awful lot of work in this area. But at the time, we did begin to do a lot of work in this area.

Q. Look over --

A. By the way, if you'll remember in the last document, Doctor Robertson, I believe --

Q. Robertson.

A. Had some -- had some "buts" in it -- but. "Looks like good work -- but." And researchers always do that, by the way. They say, "we can do it better."

Q. I understand. Look at -- look at Roman Numeral V. "Impact of Known Compensatory Behavior on Cigarette Smoking." I'm sorry. Let me read it correctly. It's V. "Impact of Known Compensatory Behavior on Cigarette

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Rankings."

A. I haven't found it.

Q. Okay. It's several pages in.

A. Roman Numeral V?

Q. Yes. It's off to the left.

A. Uh-huh.

Q. It says, "Based on the result of studies similar to those summarized above, it has been stated that low tar smokers use their cigarettes differently than smokers of higher tar products. Different usage includes propensity to block vents or otherwise manipulate the cigarette, increasing the number of puffs and the number of cigarettes smoked, puffing more frequently or with larger volumes and inhaling more deeply or holding smoke in the lungs longer. These usage patterns are consistent with the theory that low tar smokers seek to maintain a given nicotine level in the body, regardless of the cigarette. The patterns cited are instances which would tend to increase the dosage of nicotine to the smoker."

Do you see that? Were you familiar with those concepts?

A. Yes, in general, of course.

Q. Let me ask you to describe for the jury, if you could, Doctor DiMarco, what they're talking about when they're talking about these vent holes. What is the

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technology of creating a low tar nicotine cigarette that has vent holes?

A. You can -- you can alter the tar in nicotine or the nicotine in cigarettes several ways: one: by the tobacco you pick; Two: by the sheet in which you incorporate; and three: you can dilute the smoke, such that the smoker smoked the cigarette the way it's supposed to be smoked, would get more air and less tobacco -- less tar.

Q. All right.

A. And you can remove the filter, too, by the way. I mean, I had friends who didn't like low tar cigarettes and they just removed the, you know, cut the -- took the filter off. Literally.

Q. And that would be a misuse of the product?

A. Well, I don't know. People -- "misuse" is a funny word. It would be unintentional use of the product probably --

Q. That would not be the way that -- that Reynolds intended the product to be --

A. I would -- yeah, I would think it would be.

Q. -- that -- that you sold non-filtered cigarettes, as an example.

A. Sure we did.

Q. And so to cut off the filter of a low tar nicotine cigarette was not how Reynolds intended it to be

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used.

A. No, of course not.

Q. Was -- but this other description of conduct of smokers blocking the vent holes. Is that intentional or unintentional in your view?

A. My view it would be intentional, yes?

Q. It would be intentional.

A. Uh-huh.

Q. Let me ask you this. Is it possible to design a low tar cigarette which you could not block the ventilation, too, or it doesn't require ventilation holes in order to achieve the low tar low nicotine process.

A. We produced one.

MR. MARPLE: Objection.

Q. BY MR. MCCLAIN: You did produce one.

A. Called Premier.

Q. We'll talk about Premier shortly.

Was there any reason technologically speaking that products could not have been manufactured which would -- of all types, which would have prevented persons from blocking the ventilation holes in the low tar, low nicotine, the so-called low yield cigarette family?

A. I don't know of any, personally.

Q. Why not? Why weren't they manufactured that way then?

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A. I suspect --

MR. MARPLE: Objection. Go ahead.

A. I suspect it had -- if we knew how to do it, we would. If we knew how to have a smoker smoke the way we intended a cigarette to smoke, we would have done that. So I'm assuming we just didn't know any other way to do it other than ways I mentioned.

Q. BY MR. MCCLAIN: What I'm concerned about is that you say that in regard to Premier -- which was a product that was designed to reduce the delivery of tars and nicotine to smokers. Am I right?

A. Uh-huh.

Q. -- you had a product which could not be manipulated by the smoker to get more tar and nicotine. Am I right?

A. That's right.

Q. Why --

A. Produced, by the way, much later in a product we attempted to market.

Q. Yes.

A. You know, we didn't know how to do it when this thing was drawn up.

Q. Well, tell me, in regards to these holes. These perforations, they are in between the filter and the tobacco. Is that correct?

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A. No. Normally part of the filter.

Q. At the end of the filter.

A. Sometimes. Often if -- if you're going to dilute a whole lot, you dilute -- you have to have a lot of air. And you might start right at the cigarette, right at the tobacco, and just produce perforations, as I remember, pretty far up the line. If you're going to produce a mild reduction, you wouldn't need that many holes.

Q. Let me just ask you. Let's talk about some ways that you could -- assuming the smoker's not trying to block the holes. Were there any directions about how to use the cigarette given that you recall?

A. Not that I recall.

Q. In other words there was no direction, "do not block air holes," with direction to them?

A. I told you I smoked a low tar cigarette for a long long time, and I didn't get any direction. And I didn't block the holes. Nor did I rip the filter off.

Q. Well, you're a Ph.D. scientist --

A. Oh, that doesn't help at all.

Q. -- who study --

A. Believe me, that doesn't help at all.

Q. -- study tobacco all the time, aren't you?

A. No, I'm not. I'm no more that.

Q. I'm not sure you're the best example.

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A. Well, I don't know that I'm not. I really -- I mean that very seriously. Remember, I was in the business of giving Ph.D.'s out for a long time, and that just makes you a specialist in -- there's a certain way to do research in certain fields.

Q. Well, we're a little far afield. The issue is, were there any directions given?

A. I don't -- I don't know of any, but there might have been.

Q. That if it hadn't been done, would be one thing you could do to try to improve the use of the product as it was intended to be used. Am I right?

MR. DAVIS: Objection.

MR. MARPLE: Let me object to that question as well.

Q. BY MR. MCCLAIN: Isn't that right?

A. Isn't what right?

Q. That directions could help direct people on how to use the product?

A. As I told you, I just did --

MR. DAVIS: Objection.

A. -- it naturally. To me, it was natural. I mean, to me, to smoke a cigarette deep in your mouth, that you would have to smoke it to block the holes would be unnatural. So I don't -- I didn't need any instructions.

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Q. BY MR. MCCLAIN: What about putting your finger over the holes?

A. You couldn't affect it that much with fingers, because there's holes all around it. All around the cigarette.

Q. It says that "Different usage includes a propensity to block vents or otherwise manipulate the cigarette increasing the number of puffs and the number of cigarettes smoked puffing more frequently or with larger volumes and inhaling more deeply or holding in smoke in the lungs longer."

Was there -- was there no technology that you could devise at that time to prevent this?

A. Not that I knew of.

MR. MARPLE: Objection.

Q. BY MR. MCCLAIN: What was the Premier? What was the Premier technology that was invented which prevented this from occurring?

A. I just --

MR. MARPLE: Objection. Go ahead.

A. We didn't burn tobacco in Premier at all.

Q. BY MR. MCCLAIN: It was heated?

A. It was heated through an artificial source, yeah. But we didn't burn tobacco.

Q. All right. And so --

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A. So we didn't have that problem.

Q. So the ventilation holes were not needed?

A. That's right. Just the reverse probably. We'd love to get more flavor back.

Q. Look over at page -- at page --

A. Page?

Q. It's unmarked. It begins, "Evidence is available to lend support to the contention that smoker -- smokers' puff volumes are higher." It's -- it's at the bottom, the Bates Number 4507. On this side. Can you find it?

It says, "Evidence is available to lend support to the contention that smokers' puff volumes are higher and puffing is more frequent than currently specified in the F.T.C. smoking test. Further, different puffing patterns have been observed for smokers of low and high tar cigarettes. If these differences were incorporated in the standard test method, cigarette deliveries would increase relative to current F.T.C. results. If different smoking patterns were used for low and high tar products deliveries of some low tar products would increase relative to those found for the higher tar brands."

Was that something that you knew about when you were the Director of Research? That subject.

A. Let's make it clear. I don't know why this

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was written, I don't know who wrote it, and I don't know when it was written. But we knew that people smoke cigarettes differently. And early in our tenure, when we began to sell a lot of low tar cigarettes, we decided to investigate this in-house, and spent a lot of time and money doing just that. By the way, I was one of the subjects.

Q. Look at the last page of this document before the charts.

A. The next page. Yeah, all right, "Modification."

Q. Yeah. It says, "In view of these facts" -- the last sentence. "In view of these facts, the only responsible action is to educate consumers regarding the meaning of the current F.T.C. delivery rankings."

What efforts were made by Reynolds to do that that you're aware of?

A. Where are you, by the way, I'm -- if you're only reading a sentence, I want to read the paragraph.

Q. You can.

A. Where are you?

Q. "Modifications to the F.T.C. tests to achieve realistic cigarette delivery rankings," that's where it is.

VIDEOGRAPHER: Counselor, while he's reading, can we change the tape and take a couple minutes break?

MR. MCCLAIN: Sure. Yeah, we can.

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VIDEOGRAPHER: Off the record at 3:05.

(Off the record)

(Back on the record)

VIDEOGRAPHER: The time is 3:15. This begins Tape 3 for the deposition of Doctor G. Robert DiMarco.

Q. BY MR. MCCLAIN: Doctor DiMarco, do you see at this -- on this last page. "In view of these facts the only responsible action is to educate consumers regarding the meaning of the current F.T.C. delivery rankings."

Do you know of any effort?

A. I don't. By the way, I personally don't have a problem with that statement. I don't know how you would do it. And I really believe that people knew they were compensated. But I have no problem with that statement and I have no -- I don't know of any effort made by any of the companies or the government, by the way, to accomplish that.

Q. Let me show you what we'll mark as Exhibit --

MR. MARPLE: Twenty-seven.

(Plaintiff's Exhibit 27 was marked for identification.)

A. Again, we have no idea who produced this or when. According to the, I mean --

Q. BY MR. MCCLAIN: It doesn't -- it doesn't identify itself. No, we don't.

A. Okay.

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MR. MARPLE: May I inquire if this was one submitted to the court for a ruling?

MR. MCCLAIN: I don't know -- I don't know that it was claimed as privilege, was it? It's listed as *Burton* Exhibit 119.

MR. MARPLE: Okay. That tells me the answer. Thanks.

MR. MCCLAIN: Can you identify to and from for the witness? Do you have that information?

MR. MARPLE: I do not. We may be able to get it in a minute.

Q. BY MR. MCCLAIN: Do you recognize -- the question I have is do you recognize this, Doctor DiMarco, as something that would have been prepared by the Research Department?

A. I'd have to read it.

Q. Let me ask you, were a number of studies developed for the production of Premier cigarettes?

A. Were a number of studies performed?

Q. Yes.

A. Oh, yes.

Q. Would you look at this document and see if you recognize it as being one of those studies that was a precursor to the development to Premier?

A. To answer your first question, I don't know

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if -- this doesn't read to me like a research document. The second question, I'm still trying to evaluate. I can tell you my own perception of how we came about Premier, which would have nothing to do with this, I mean.

Am I back at the beginning?

Q. No, you're --

A. I took the clip off.

Q. No, you need to go down to --

A. Oh, I see. "Key Issues."

Q. This appears to be a Power Point or slide presentation that was given to some group.

A. Yeah. I'm not surprised about it, but I just don't --

Q. Just don't know anything about it.

A. I don't know anything about it, nor do I think it was produced by researchers. It just doesn't read that way. But I have no problem with what it says, at least from what I've read so far.

MR. DAVIS: Is there a question?

BY MR. MCCLAIN: My only question was did he recognize it or does he recognize it. Can you ask who this is to and from, Bill?

MR. MARPLE: We'll try to find that out.

MR. KREINER: What's the number?

MR. MCCLAIN: One-nineteen. *Burton* Exhibit 119.

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He's going to tell us who the documents are to and from?

MR. KREINER: It's not -- so I don't have it.

MR. MARPLE: I'm sorry. We don't have it, I guess.

MR. MCCLAIN: All right. Let's mark this then.

Q. BY MR. MCCLAIN: Let's set that aside, Doctor, since we don't know anything about it and you didn't have anything to do with it.

(Plaintiff's Exhibit 28 was marked for identification.)

MR. MCCLAIN: Was it marked?

COURT REPORTER: I'm sorry.

Q. BY MR. MCCLAIN: This document is entitled "Proposed Biobehavioral/Brand R&D Cooperative Projects." That was your department, wasn't it, Doctor DiMarco?

A. Are you asking did biobehavioral report to me? Yes, it did.

Q. And brand R&D cooperative -- or brand R&D, that was what department?

A. We had a brand group. Now, whether that's -- whether this refers to marketing or ours, I don't know. Brand R&D would be ours, obviously, yeah.

Q. Do you recall the proposal to test Camel Light and Merit "nicotine spiked cigarettes"?

A. Where are we?

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Q. Three.

A. No, I don't. I'm surprised they used the words "nicotine spiked" for Merit.

Q. Look -- look back at Page 5 of this document.

A. (Reviewing document.) Do you just want me to look at that one page?

Q. Yeah, I did. I just want to ask you a question. It says -- this is -- the subject is, "The test of Camel Light and Merit nicotine spiked cigarettes with D.F.C., smoking behavior measurements, and replicated human smoking." It says, "What is it? - Nicotine deliveries of Camel Light and Merit will be raised by injection of nicotine into filters. Sixty-member panel would be divided equally among two or more versions of each cigarette." And then it drops down, "Why do we want to do it? It is known that nicotine delivery can be conveniently manipulated by filter injection."

What do they mean that "the nicotine content can be manipulated by nicotine injection into the filter"?

A. Are you asking what I think this means?

Q. Yes.

A. We never injected nicotine into the filter, by the way, ever. But it would be a way in which they could control the amount of nicotine a smoker's going to get. And this is a research proposal to learn something. It's not a

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proposal -- a research proposal to produce a new product, which is not unusual, by the way, in any research organization.

Q. What would be learned by it?

A. They say here whether nicotine, I guess -- the effect of nicotine from a biobehavioral point of view, since it's coming from that group. The work would be done certainly in biobehavior.

Q. Is it fair to say --

A. By the way, they're not cigarette makers either. They're learners, they're researchers.

Q. Is it true that a number of attempts were made within research to adjust the nicotine content of the cigarettes?

A. If you mean by "adjust" --

MR. DAVIS: Objection.

MR. MARPLE: Let me object to that as being ambiguous.

A. I was going to ask you --

Q. BY MR. MCCLAIN: Have you understood my question?

A. -- what you mean by -- I say, if you mean by "adjust," yeah, within the limits imposed, you know, to -- you would then test if whether it improved your product or did not.

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Normally, you cannot just manipulate nicotine. You have to manipulate nicotine, tar, and construction in general.

Q. What was Project X.B.? Do you recall?

A. No. We had all kinds of numbers. If you could refresh my memory, I probably could.

Q. I'll give you a document that you're -- on --

(Plaintiff's Exhibit 29 was marked for identification.)

Q. BY MR. MCCLAIN: Are these questions you were asking?

A. I don't recall. I don't think I'd have enough knowledge to ask most of them. Did I write this, or was it copied --

Q. It bears your initials -- Huh?

A. I don't know whether I wrote it or it was copied. It doesn't make any difference, does it?

Q. It's 1990. It says, "How much nicotine do we need in a five-milligram product to satisfy normal smokers?" And then is that -- whose writing is this?

A. It's not mine.

Q. "Plasma data .6 smoke nicotine." See where it says --

A. (Reviewing document.) "...the total do we need to get the proper organoleptic feel." Let's do it all.

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Q. What does that mean?

A. It means that nicotine alone does not determine desirability. It has to have a mouth feel and a taste that satisfies a consumer as well. In fact, in my opinion, and the opinion of most in this field, the organoleptic feel is the predominant way people choose to smoke a given brand at a given tar level.

Q. And that's determined by free nicotine?

A. No, no. It's determined by mouth, feel, taste, nicotine. Anything you could say about a cigarette.

Q. It says, "How much free nicotine of the total do we need to get the proper organoleptic feel?", correct?

A. That's -- that's right. That's --

Q. That was the inquiry?

A. That was the inquiry. But that reads to me as a researcher, we -- you know, that's a variable that we'd like to have a handle on, because I certainly know what a organoleptic feel is -- organoleptic feel to --

Q. Number 6 --

A. That's a variable that you would want to know about. Along with lots of others.

Q. It says, at Number 6, "How good do we feel that Legal group will allow us to sell product we visualize - i.e., take out tar verses add nicotine."

A. "How good do we feel that Legal group will

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allow us to sell" -- actually, Legal group doesn't make that determination.

Q. "Take out the tar versus add nicotine."

A. Well, you can't do that. It's impossible.

Q. I'm only reading what it says.

Q. Well, I'm telling you, whatever it says, you can't do it. I told you before you have to have a given ratio in order to be able smoke a product. That's one reason why we took nicotine out of tobacco.

Q. So --

A. Now, this might be referring -- I have no idea, because I don't remember, to Premier. I'm not sure.

Q. That's from --

A. The difference being --

Q. 1990 --

A. -- you know, the difference being that -- oh, yeah, we were working on Premier then.

The difference being that Premier didn't deliver tar at all. We didn't burn tobacco so we didn't deliver tar, and that's one of the reasons why we had so much problems with the organoleptic feel of Premier.

Q. What did you --

A. By the way, I have to believe that this is Premier. I'm not sure, but I have to believe it.

Q. What -- let me just stop you for a minute and

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ask you. You were very involved with Premier?

A. Absolutely.

Q. It was probably the most significant project of your career at Reynolds. Am I right?

A. I'd like to believe we had some others that are going to be even more significant.

Q. At the time it was one of the most significant projects?

A. There's no question.

Q. You were proud of it?

A. I loved the effort. I loved the effort, yes. So did lots of other people, by the way.

Q. Do you smoke them?

A. You better believe it.

Q. And you liked them?

A. I learned to like them.

Q. They were --

A. That was one of the problems with them.

Q. They were -- they had to be learned to like?

A. You can understand my motivation for learning to like them.

Q. Yes. But you did learn to like them?

A. Well, I did over time.

Q. And they had reduced tar --

A. Uh-huh.

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Q. -- didn't they?
A. Essentially no tar.
Q. And --
A. As we know it.
Q. And reduced nicotine?
A. Reduced nicotine as we know it.
Q. And Reynolds withdrew them from the market. Am I right?
A. Uh-huh.
Q. In your view, Doctor DiMarco, it's fair to say, isn't it, that you had hoped that the company would stay with the product longer. Isn't that true?
A. Yes, that's true.
Q. And you had some belief that if they would do that or hoped, anyway, that other consumers would have learned to like them.
A. That's true.
Q. Because you believed that this product which you had worked on for so long, that had essentially no tar and no nicotine was a more responsible product to sell to consumers of cigarettes. Am I right?
A. I would word that differently.
Q. Okay. Tell me how you would word it.
A. When -- if I might. Before we started on the project, I went to every public agency and said, "Look, we

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would like to reduce the risk -- a risk factor that cigarettes play, and everything they've been accused of playing. What do you know that I can do to that product? What can I take out from that product?" What could I do, because we wanted to know, all of us did, what we could do. And they all said, "We don't know anything. Since we don't know how or if we don't know anything."

So it was a decision of the group, what we'll do is take everything out. As much as we could. And that is essentially what we tried to do. We know, the world knows, because it's in the literature, that when you burn things and you don't get complete paralysis. Yeah, you get active products; products are biologically active. That's why I talked about steak some hours ago, especially if it's charcoal. We knew that.

So we attempted to produce a product that people would like that would reduce the so-called perceived risk of smoking. And the only way I knew to do that or we knew to do that was to take everything out.

Q. And that's what you did with Premier?

A. We tried to do that with Premier, yeah.

Q. To the extent ---

Do you remember what the tar and nicotine numbers were?

A. There were no tar numbers that I remember

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because we didn't burn tobacco. Tar, by definition, is a product of combustion.

We -- we tried to flavor it to match the flavor of the burned tobacco. In the end we didn't know how to do that. We used one of the largest companies in the world, Fermanich, by the way, in Switzerland, to help us do that, and they couldn't help us very much either. Spent years at it. So we were never able to accomplish that piece of it. I felt that if we could accomplish that piece of it, yeah, we'd have a product out there that people would enjoy, but without it it took too much getting used to.

Q. Now, let me -- let me just ask you a philosophical question.

A. Uh-huh.

Q. Very few smokers like the taste of cigarettes when they start. Isn't that right?

A. I don't know that. I loved the taste.

Q. You've heard that, haven't you?

A. I don't know that I've heard that.

Q. That it takes time to learn how to smoke. In fact, in Doctor Teague's memo he talks about that.

A. Yeah, but I told you I probably never saw that memo. I don't know that. People tell me that it takes -- that you have to get used to smoke -- to drinking scotch. I love the taste of scotch. I don't know that I've learned

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to. I did learn how to smoke Premier, by the way.

Q. Yes. And it's true, isn't it, from your standpoint that if Premier could have been --- strike that.

In terms of your concerns that ---

You expressed from the time you came to Reynolds to the time you left that Premier was superior to the cigarettes that you were offering in terms of its ability to deliver components that were of concern to you in the Research Department to smokers. Am I right?

A. We've got to take that question apart. From the time I came to the time I left, because when I came we had no idea that Premier would exist. We had to invent that, and it took some time. As a matter of fact, it took a lot of time and many, many, many, millions of dollars.

But I think I said before -- in fact, I'm sure I said before, I knew the company wanted to produce a product that would be, based on all the knowledge we had, reduce risk -- a reduced risk product. Now, you will remember that somebody was talking about my concern for reduced safety. Well, that's a word that confuses a lot of people, and lawyers don't like, so I stopped using it.

There is no question that when you -- it's in the literature; it's all over the literature -- that when you smoke a Premier you get less mutagenicity in the product of the smoke than you do with regular cigarettes. There's

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no question about that. And we think that that reduces the risk, whatever the risk might be, vis-a-vis, smoking.

And I started to say, and I should complete that, the company wanted to do that before I joined it. That's one of the reasons I did join. I said, you know, this is a very responsible company, they just built a brand new research facility, unbelievably modern. They're obviously committed to research; and, therefore, I came. I didn't have to come. I had a beautiful job.

Q. Now, let me stop you for a moment. How many years was Premier marketed?

A. Gee, I'm guessing two or three years.

Q. And how many markets was it offered?

A. It was offered in as many test markets -- in fact, more test markets than you would normally use for a regular cigarette because we had a lot to learn. That's not unusual, by the way.

Q. Was it ever offered throughout the country as opposed to just in test markets?

A. No. They had no reason to do that.

Q. And so it was never offered to the entire smoking public on a nationwide basis. Is that right?

A. That's exactly right.

Q. And, in fact, the company, R.J. Reynolds Tobacco Company, went through a buy out at about that time?

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A. God knows. They were not easy times for me, but I suspect that's about the time that -- that K.K.R. bought the company.

Q. K.K.R.?

A. I think they were the group that purchased the company.

Q. The leverage buy out firm? And --

A. If that's what you call them.

Q. And it was following their takeover that the Premier project was killed?

A. It was never killed. To this day we're still working on products of that nature. So it was never killed, if that's what you mean.

Q. Are you still doing work on Premier?

A. I don't know. If I had to bet my life I'd say, yes, we're doing work on a product like Premier.

Q. But you're not doing any specific work for Reynolds Tobacco at this time?

A. No, I'm not.

Q. But it was at or about the time of this buy out that Premier --

A. I think so.

Q. -- worked on --

A. I'm not sure, but I think so.

Q. -- Premier ceased. Were there other cost-

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cutting measures that were brought into play at the Reynolds Tobacco Company following this buy out --

A. Wait a minute --

Q. -- by K.K.R.?

A. You just make an assumption which I think is invalid. You're assuming that when K.K.R. bought the company, they cut my research budget. That's simply not true.

Q. They did cut the promotion of Premier.

A. Yeah, but for a different reason. It had nothing to do with cost-cutting. Nothing to do with cost-cutting. We continued to work on Premier until the day I left, and I'm sure they're working on it today. I bet my life on it.

Q. Well, let me ask it this way. They didn't cut your research budget --

A. No, they didn't.

Q. -- but they didn't budget money to market Premier, did they?

A. After the decision was made to pull it for valid reasons.

Q. All right.

A. For very valid reasons.

Q. Reasons that you disagreed with.

A. Reasons I couldn't argue with, but I did

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argue, because that's my nature.

Q. You argued against pulling it.

A. Absolutely.

Q. You thought that they hadn't given it a sufficient chance?

A. No, I didn't say that.

Q. What did you say?

A. I said I argued against pulling it, and I said that's normal and natural when you have a baby that you thought you played a role in, a relatively large role, that, yeah, you didn't want it hurt.

Q. What arguments did you make?

A. Well, but you see, what -- it sounds to me that you have no idea why it was pulled. You're acting like we pulled it for cost reasons.

Q. I want you -- I want you to tell me what argument you made against pulling it, and then you can tell me whatever you want about pulling it.

A. My argument is very simple. I knew the person who introduced the no-sugar, low-sugar soft drinks.

Q. Yes.

A. Doctor Bill Miller, Royal Crown, personal friend of mine. He said it was horrible. And he argued with his company that what you have to do is leave it out there and learn. And over time, over a long period of time,

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that's exactly what they did.

Q. And that's a very good analogy, isn't it? The original -- the original --

A. Well, that's what I argued. But that doesn't say there weren't, in fact, other factors involved in Premier: i.e., American Health, American Lung, American Medical Association, all came out and said, "You've got to get that product out of the marketplace."

They not only went to us. They went to F.D.A. and made a very strong plea, as strong as you can make it, that that product was not a product that should not be in the marketplace.

Q. Well --

A. F.D.A. said, "We agree."

Q. So it's your testimony that F.D.A. banned the product?

A. F.D.A. did not ban the product. F.D.A. let us know in uncertain terms that these are very responsible groups who have been fighting to get this product off the market, and we agreed with them.

Q. Well, F.D.A. had no jurisdiction over your company, did they?

A. They have the jurisdiction anytime they want. We are probably more regulated then even the milk industry, which is very highly regulated.

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Q. Well, do you know whether the F.D.A. had any control over your company? Did they -- did they --

A. F.D.A. had control in whether that product stayed on the market or not, or at least could fight its being on the market.

And if you -- I don't know whether you remember or not, the pressure out there from very legitimate groups, by the way. I personally took that product, with the dean of a medical school, to the A.M.A.; I took it to Harvard Medical School; I took it to lots of places; we took it to lots of places, and they all agreed, "Hey, that's a pretty good product."

But in the end, for whatever reason, they chose -- I have no idea what the reasons are. I'll never understand it. They came out against the product. They fought us in the marketplace, by the way, with everything they had, and they fought us at all government agencies they thought that could prohibit us from marketing that product. And all that pressure along with the fact that consumers didn't like it ended up in the product being pulled.

Q. Doctor DiMarco, let me ask you this. It's true, isn't it, that the tobacco companies are frequently opposed by the American Medical Association, the American --

A. Lung.

Q. -- Lung Association?

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A. They don't oppose everything we do.

Q. Don't they nearly oppose everything you do?

A. We used the president of the American Lung Association as a chairman of our committee who chose good scientists throughout the world who we thought we could support to get started, and he did it gladly.

That group -- those groups, I believe, was represented in a group that came down to see us after the fact, and said, you know, we were after people to stop smoking by the year 2000. That's really not -- obviously did not happen. I was not with the company at the time, by the way. It was reported to me, and I better make that clear, and they said they think they made a mistake in opposing that product.

Q. Well --

A. That didn't stop us from working on a product, by the way. I said I'd bet my life on the fact that they're working on it diligently today, and you know we're in test market right now with a product very similar to it.

Q. What's it called?

A. It's called Eclipse.

Q. Let ask you -- let me ask you this -- come back to my point. It's true, isn't it, that the American Lung Association, the American Health Foundation have

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frequently opposed actions Reynolds has taken in regards to cigarettes?

A. American Health Foundation? I didn't say that. American Heart, American Lung, A.M.A. -- American Health Foundation, I personally knew the director and he was with this product one hundred percent. He was the fellow that discovered filters, by the way. Well, he claims he discovered filters.

Q. So there were people in the market ---

There were people in the scientific community supporting Premier?

A. Uh-huh.

Q. Regardless, it was pulled.

A. Can I -- yeah. I'm trying to remember his name. He is -- I should know it like I know my own. But I can remember sitting in his office and saying, "Hey, look, will you tell the world what you just told me, vis-a-vis, this product?"

And he said, "Absolutely, I will, if you will guarantee me that you will make up every dollar of Federal Research I'm going to lose if I do that."

And I said, "I can't guarantee you that." And so he, of course, didn't say what he told me privately. It's a tough world out there, friend.

Q. Doctor Hoffman or Doctor Wynder?

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A. Doctor Wynder. I knew Doctor Hoffman, too. Very good scientist, by the way.

Q. Is it Doctor Wynder who told you that?

A. Yeah. He's either retired or --

Q. He's passed away.

A. Is he passed away? Certainly not John.

Q. What was X.G.T.?

A. You remind me. I have no idea. Remember, you're talking about symbols used by --

Q. It was the nicotine -- nicotine --

A. We used symbols for everything. I couldn't keep track of them when was I was there, let alone ten years later.

Q. Let me show you this -- let me show you this document.

(Plaintiff's Exhibit 30 was marked for identification.)

A. (Reviewing document.) It still doesn't tell -- I've just read the first page -- but what X.G.T. -- okay, I know what it is.

Q. BY MR. MCCLAIN: What was this about? Do you recall? What was the nature of that study?

A. It tells you clearly on the first page, first two paragraphs. "Technology to allow R.J.R.T. to manufacture reduced delivery cigarettes with smoking

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characteristics (taste, satisfaction) comparable to products with substantially higher delivery."

Q. Is this a project that you recall?

A. I certainly was aware of it, but I don't remember the details. But I wouldn't be expected to.

Q. And was this -- was this technology, in fact, put into place?

A. Never during my tenure. Only because we didn't know how to do it, as she says here.

MR. MCCLAIN: Mark this. (Handing document to assistant.)

(Plaintiff's Exhibit 31 was marked for identification.)

A. My interest, by the way, as I recall in this project, was what was said here at the bottom of the page, "Can be used for new generation products, as well."

Are we off of 20 -- 30?

Q. BY MR. MCCLAIN: Yes. I want to come back to your discussion of Premier.

A. (Reviewing document.) I was not at this meeting, by the way, but I have met with Doctor Weisburger before on several occasions. I have a great respect for him.

Q. And was this -- was this a meeting regarding the Premier cigarette?

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A. I haven't read it yet.

Q. Okay.

A. (Reviewing document.) You know, I could take another ten minutes reading this. If you give me your question, I'll try to concentrate --

Q. This is about Premier, isn't it?

A. I'm quite sure it is.

Q. The Alpha project. This project was Premier. All right. It says -- just so that we can -- I should have given you this document before I jumped on the Premier subject, just to lay out the framework of what we're dealing with with Premier. It says -- and who is Weisburger and Associates or Weisburger and Associates?

A. That surprised me. I'm assuming this is Doctor John Weisburger, who was Research Director for the American Health Foundation. I was not aware that he had a, you know, association on his own at all. I don't know who they are. I don't think at this time that he was not part of the American Health Foundation.

Q. This is a meeting with Doctor Weisburger and the professional staff of R.J.R., right?

A. No. Yes, it is. It says -- you asked me who Weisburger Associates are. I don't know who they are. I think at this time he was the Director of Research of the American Health Foundation. His wife, by the way, at the

52649 4340

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time was in D.C. She is also a person who worked a lot with toxins.

Q. It says, "In view of the problems associated with the use of the standard smoking products in relation to risk for coronary heart disease, specific types of cancer, emphysema, and related problems in the respiratory tract, R.J.R. has invented a smoking product with a radically new revolutionary design in order to avoid many of the adverse claims associated with conventional smoking products."

That was Premier?

A. That was his interpretation of what Premier was, yeah.

Q. On the second page at the top it says, "Adverse effects have been associated with the presence of appreciable amounts of polycyclic aromatic hydrocarbons, tobacco specific nitro" --

A. Nitrosamine.

Q. -- "nitrosamines, and other nitrosamines reactive nitrosating elements, aromatic, and heterocyclic" --

A. Heterocyclic.

Q. -- "amines," right? "And acidic compounds like phenols, catechols, aldehydes, thiocyanate, and H.C.N. In great part the presence of these chemicals in the mainstream has been related to adverse effects as regards

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cancer, emphysema, and respiratory tract diseases. Recently emission of some of these products in the sidestream smoke has been of concern in relation to passive smoking. I addition standard product emit appreciable amount of CO, CO2, and nicotine. The presence of CO in part of nicotine has been thoroughly thought to be related to an increased risk of myocardial infarction, at least in individuals on a Western nutrition -- nutritional tradition."

A. Tradition.

Q. It goes on to say on the second page, "Inhalation tests in rats" --

A. Now, wait. I think you should know that in all these fancy words up here there's all these chemicals, I would venture to guess that at least ninety percent of them were discovered by Reynolds, and published in the journals through Doctor Rodgman --

Q. That those -- that those components were in cigarettes?

A. Were in tobacco smoke. Yeah. We -- we discovered them and published them.

Q. And every person that smoked cigarettes got them into their lungs. Am I right?

A. Got them from, many think, including cigarettes. But remember what I told you. I went to every learned institution I could go to to include Johnny's, by

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the way, and said, "Which one should I take out? Which one do you -- can you show me cause the problems that he lists here?" And do you know what the answer was? I told you it was, "We don't know."

Q. And that's why you reduced them all.

A. That's why we tried to reduce them all; hopefully, reducing the risk.

Q. Look over at the next-to-the-last page. It says, "The nicotine levels in Alpha products are also somewhat lower than in many standard products. However, it has been shown with standard cigarettes of varying nicotine output that smokers tend to compensate use in order to ensure certain specific blood levels. Your group has performed detailed studies in this area including mechanism studies of pharmacokinetics of infused nicotine. It appears clear that Alpha offers the user nicotine in a manner that will be not too dissimilar from that of other cigarettes but at lower level, yet sufficiently high that the alleged pharmacological requirement is met."

Was that the way that the Premier product worked?

A. The Premier product delivered no tar, as I told you, as we measure it, and delivered some nicotine at very low levels.

Q. That could not be manipulated by covering up

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the air holes or any of the other ways that you can manipulate the delivery of the conventional low tar cigarettes?

A. There are other ways in which we reduce the tar of other -- low tar cigarettes. The word "manipulate" has a connotation that I don't think is fair.

Q. Altered by the smoker.

A. No, no. That's not -- that was not your question.

Q. I've changed it to "altered by the smoker" to get over your objection.

A. No. They --

Q. Premier couldn't be done that.

A. You couldn't do that, no.

Q. Now, the summary. "The data presented on a comparison of the toxicological properties of Alpha product compared to the conventional materials lead to the conclusion that this product does not have many of the components of conventional product that had been associated with disease risk. Thus, it seems evident that the user of Alpha product will be low, if any risk for conditions that previously were of the major negative elements in users, especially problems of emphysema, respiratory tract abnormalities including neoplasia, and cancer in select other organs. In my opinion, Alpha product is a major

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technological advance based on an intimate understanding what kind of potential harmful elements had to be eliminated. Alpha product is successful, in my opinion, in meeting this goal."

And that's why you advocated to the management of Reynolds not to withdraw it from the market. Am I right?

A. It was one of the reasons, yeah. There's no question, by the way, all of this is published. You've seen it published, haven't you? Every detail that he outlines here has all been published by Reynolds both in a manuscript, a monograph, as well as, in papers. So I don't know -- that certainly not a surprise to you is it?

Q. Well, I don't know whether you want me to address this to you or not, but as you understand, all I can present to a jury is evidence. And now you're giving evidence. And what's published in some book somewhere is not. So I have to ask you the questions because you're evidence and a book someplace isn't. Okay.

A. See, I'm learning about lawyers.

MR. MCCLAIN: That's it.

MR. MARPLE: Objection.

MR. MCCLAIN: Thank you. I have no further questions.

EXAMINATION

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BY MR. MARPLE:

Q. Doctor DiMarco, I have a few questions. My name is Bill Marple, and I represent R.J. Reynolds Tobacco Company in this lawsuit in which we're here today. Can you just tell us your name, please.

A. G -- stands for Gabriel Robert DiMarco.

Q. What's your date of birth?

A. July 31, 1927.

Q. And so as we sit here today you're seventy-four (74) years old.

A. Very recently, yes.

Q. What's your educational background?

A. I have a B.S. degree from Rutgers University in research. No -- Nothing specific, just in research procedures and I got a Ph.D. from the Plant Pathology Department at Rutgers University.

Q. Briefly tell us your major employment history.

A. I had three employments. One: I became a professor at Rutgers in another department called food science, and ultimately became the chairman of that department. I think we grew with the department rather substantially -- I think history will show that, and we built a brand new facility supported by the state and by the federal government, and I decided to leave Rutgers because I

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found myself being what I call a caretaker.

And I went to General Foods. At General Foods I was the director of fundamental research, which included some product development, by the way and all the interfacing with most government agencies that dealt with food and food safety.

Q. And just --

A. After that I left and came to Reynolds.

Q. And approximately what time frame were you a professor at Rutgers University?

A. Oh, boy. Early sixties, I suspect to -- actually, I was employed by Rutgers in a different -- yeah, by Rutgers -- in a different capacity before that. Until around '75.

Q. And that's when you went to General Foods?

A. That's right.

Q. And where was that company located?

A. Located -- they were located in White Plains.

Q. New York?

A. New York. Yeah.

Q. And just approximately --

A. Just the headquarters not the Research Department.

Q. Where was your Research Department?

A. At the time I joined the company it was in

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Terrytown. And when I left it was still in Terrytown, but we had an auxiliary group down in New Jersey, in the White Plains -- I mean, off the -- I'm sorry, off the Turnpike.

Q. And just approximately how many persons were in that Research Department at General Foods?

A. It varied. Somewhere in the vicinity of -- when I left -- I tend to be a builder because I'm a believer -- I think around seven hundred (700).

Q. And then I believe you told us earlier you came to Reynolds about 1982.

A. About '82, yeah.

Q. And you retired when?

A. About '92.

Q. And when you came to Reynolds, what was your position?

A. As I said before, I was -- we had a Senior Vice-President of Research, and I reported to him. I don't honestly remember whether I was just a Director of Research or had a Vice-President title at that time. I was only in that capacity for a little more than a year.

Q. And after that approximate year period, who did you report to then?

A. The president of the company.

Q. The president of R.J. Reynolds Tobacco Company was your boss?

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A. Yes.

Q. Were any of the lawyers that we talked about today -- Mr. Juchatz, Mr. Witt, Mr. Finnegan, or Mr. Jacobs [sic] -- ever your boss?

A. No.

Q. And did you ever report to them?

A. No. I couldn't say absolutely not as I had before, but the answer is no.

Q. Did your superiors -- that is, the president of the company -- for most of the time you were there place any restraints other than through the amount of money that was granted to the Research and Development Department, place any restraints on the types of research that you did?

A. I can't remember an occasion where they said, "you cannot do that." As a matter of fact, budget -- when you do these things internally as compared to others, you know, your budget grows substantially. And I've been -- I can truthfully say that I've been tremendously supported by everybody I reported to.

Q. Did the budget for your department grow or increase during your tenure at Reynolds Tobacco Company?

A. You better believe it.

Q. And did you have an order of magnitude from what it was at the beginning and what it was at the end?

A. Certainly threefold. It might have even been

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a little higher.

Q. Was there ever an occasion when there was some research that you wanted to conduct or have conducted by people working for you where you were told you could not do that research by your superiors?

A. By my superiors?

Q. Yes.

A. No. Mind you, I had to sell programs. You don't walk into any place and just say, "Hey, I want to do this; therefore, we're going to do it," but I'm a pretty good salesperson.

Q. My question was --

A. Let me put it another way. No one ever -- no one I ever reported to said, "Hey, are you sure," based on health concerns. They might have asked based on dollar concerns, but I can never recall any of the presidents I dealt with saying no because of health concerns.

Q. And the research that was conducted during your tenure, was there sometimes written reports made of that research?

A. You write written reports of all research done, by definition.

Q. And you did that during your tenure and the people under you did that?

A. I'm sure it was done throughout the history

EXHIBIT

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of the company, yes.

Q. And certainly done during the time you were there?

A. Of course.

Q. At -- was there ---

At any time that you're aware of, were any of the written research reports destroyed? That is, the original destroyed?

A. It would be impossible to do that without my knowledge, I think. And as far as I know, none would ever do that. You just wouldn't do that. I mean, that's just part of research.

Q. Was there a depository or place where these research reports were ultimately kept or filed?

A. Yes. Normally in a fireproof situation where, in fact, you can protect them pretty well. Normally in two places, by the way. And I'm sure we did have two places.

Q. And are you aware -- were any of them eventually placed on microfilm?

MR. MCCLAIN: Object to the form of the question. It's leading.

Q. MR. MARPLE: You may answer.

A. Yes, they were. I think we kept both versions, however.

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Q. Was there ever a time during your tenure when any of the research scientists working under you came to you and told you that someone in the company had told them that they could not conduct the research that they were conducting?

A. I want that question clarified, too. If you're -- if you're asking did anyone ever say that they couldn't conduct something that they thought we -- we'd agreed to they could discuss, and were not allowed to, the answer is no. They were always allowed to do what we said we were going to do. Now, whether someone told them something else, it doesn't make a difference to me.

Q. Did anyone at the company ever prevent the scientists working in the Research Department, during your tenure, from publishing material that you and the Research Department thought should be published other than for some patent or proprietary reasons?

A. No, they have not. We have held up publications, as I've said before, until they were patented and then, of course, published.

Q. And that was something where ---

Or am I to understand that if it was something that was going to be patented, that information would be submitted to the Patent Department or the U.S. Trademark Office, whatever it is?

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A. Patent Department, yeah.

Q. And they review it.

A. Most patents, by the way, are considered publications, because they not only review it but if they approve it, they publish it.

Q. That's right. And if the patent, for whatever the process or product is is granted, then the full patent describing everything about that gets published.

A. Gets published, of course. That didn't mean we didn't publish it in a referee journal after that, because you are allowed to do that.

Q. You mentioned the term "referee journal." Is that what I heard you say?

A. Uh-huh.

Q. Can you tell us what you mean by "referee journal"?

A. It's a journal where peers evaluate your work and decide whether it's worth publishing or not. They sometimes will come back and say, you know, "This is not clear, would you clarify this for me or clarify that for me." But the judgment as to whether it will be published is made by peers. It's not foreign at all to researchers. That's what we do.

Q. There were some questions earlier about nicotine in cigarettes and whether nicotine was added or

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taken out through various processes. Do you recall questions about that?

A. Yes, I do.

Q. Can you tell us whether there ---

Were you aware that there was ever a product -- a cigarette product sold by R.J. Reynolds Tobacco Company that contained more nicotine than that that occurs naturally in tobacco?

MR. MCCLAIN: Object to the form of the question. It's leading.

Q. BY MR. MARPLE: You can answer.

A. I can answer. You have to qualify that, because you can produce cigarettes that have a lot of nicotine in them. We would never produce them because people wouldn't smoke them. So I'm really asking you to clarify your question.

Q. Are you aware that there were ---

Are there processes ---

Strike that.

Are there processes that Reynolds used that resulted in lowering the amount of nicotine in the cigarette, lower than that that occurs naturally in tobacco?

MR. MCCLAIN: Object to the form of the question. It's leading.

A. If you're talking about -- I think you're

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talking about, have we ever taken nicotine out of tobacco? And the answer is yes, we did that routinely.

MR. MARPLE: I believe that's all I have. Thanks.

EXAMINATION

BY MR. MCCLAIN:

Q. Doctor DiMarco, I just have a few.

(Plaintiff's Exhibit 32 was marked for identification)

Q. BY MR. MCCLAIN: This document, you'll see, is from July 20, 1982. It's to Doctor Roy Morse from Frank Colby -- Colby, and you're copied on it down at the bottom, C.D., D.J.M. In this, Mr. Colby reports on a unpublished study that B.A.T. -- British American Tobacco -- did on using baboons to test coumarin. Am I right?

What is coumarin?

A. Gee, coumarin is, I think a spice -- spice.

Q. And was it utilized in cigarettes?

A. Not to my knowledge. Could have been but I don't remember it ever being used.

Q. Would you look at the directions from Mr. Colby that, "It's important that the fact that we have knowledge of this unpublished study be kept strictly confidential."

A. I see what it says.

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Q. And that Mr. Colby was incredulous that both Imperial Tobacco and B.A.T. had approved this study and that, "At this time it's impossible or difficult for me to obtain additional information. This is mainly because the study was commissioned by both Imperial and B.A.T."

MR. MARPLE: Objection.

A. That's what it says.

Q. BY MR. MCCLAIN: Do you know why you were copied on that study? Or why Mr. Colby thought it must remain strictly confidential?

A. I can tell you that studies on coumarin, per se, were not confidential. They're in all of the literature. That's why I have some recollection of it. Whether, in fact, this particular study was -- was in the literature, I don't recall, but coumarin has been all over the literature for a long time.

Q. All right. Now, let's talk about research reports.

MR. MCCLAIN: Put it over that trial sticker. You don't need that.

(Plaintiff's Exhibit 33 was marked for identification.)

Q. BY MR. MCCLAIN: Do you know Mr. Max Crohn?

A. No, I do not -- didn't know him -- don't know him.

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Q. "Invalidation of Some Reports in the Research Department."

A. Never saw this.

Q. Let me read it to you. "We do not foresee any difficulty in the event a decision is reached to remove certain reports from research files. Once it becomes clear that such action is necessary for the successful defense of our present and future suits, we will promptly remove all such reports from our files."

Were you ever aware of this memorandum?

A. No way. I can't believe it. I don't know who he is.

Q. He's from the Legal Department. Max Crohn.

A. He was not a member of the Legal Department in my tenure.

Q. Mr. Rodgman -- Doctor Rodgman has identified him as being a member of the Legal Department when he was there.

MR. MARPLE: Objection.

MR. DAVIS: Objection.

MR. MARPLE: Object to the conclusion.

A. He certainly wasn't a member --

Q. BY MR. MCCLAIN: Did Doctor Rodgman tell you how incensed he was when he discovered this memorandum in the litigation?

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MR. MARPLE: Objection.

A. No, I certainly don't recall.

Q. BY MR. MCCLAIN: And how these were his reports?

A. I can't believe they were removed.

Q. You didn't understand. You have no knowledge of this?

A. No.

Q. So when you were answering Mr. Marple's questions, you had no understanding about this entire incident. Am I right?

A. No. We talked about my tenure.

Q. Yes.

A. And I said no, we never would --

Q. So you had --

A. -- this is not my tenure at all --

Q. All right.

A. -- and I'll be surprised if it happened under any tenure. You just don't do that with research reports.

Q. It says, "As to the reports" --

A. I don't care what it says. If you've got a Research Director who's worth his salt, he's not going to let that happen.

Q. Well, who was the Research Director before you?

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A. I have no idea. Oh, Doctor Roy Morse. He would never -- no way.

Q. It says --

A. About the other, I told you I only know casually. I also told you when I joined the company we had some very, very, fine scientists there. Rodgman was one of them.

Q. Pick the document up, if you would, because I want to ask you about this.

A. Why do you want to ask me something that I had nothing to do with?

MR. DAVIS: It's okay, Bob, just --

Q. BY MR. MCCLAIN: Counsel asked you about this. I didn't raise it, remember? I didn't ask you anything about destroyed documents. He did.

"As to the reports which you are recommending to be invalidated, we can cite misinterpretation of data as reason for invalidation. A further reason is that many of these are needless repetitions and are being removed to alleviate overcrowding of our files."

Do you see that?

A. I see what it says.

Q. "As an alternative to invalidation, we can have the authors rewrite those sections of the reports which appear objectionable."

Original Illegible

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Did you know that the Legal Department ever recommended that?

MR. MARPLE: Objection. Calls for speculation.

A. The answer is no.

Q. BY MR. MCCLAIN: And then let's talk about your tenure.

(Plaintiff's Exhibit 34 was marked for identification.)

Q. BY MR. MCCLAIN: November 16, 1983, you were Director of Research, right?

A. I don't know whether I was a director or still reported to Doctor Morse. But I don't know whether it makes any difference in the conversation.

Q. It says, "The following lists of formal reports were issued to Alan Rodgman, and have been destroyed." Isn't that what it says?

A. These reports, that's what it says.

Q. Were you unaware of this?

A. Wait a minute now. Wait a minute now. It doesn't say that the original reports were destroyed. In fact, I'd have to bet my life that the original reports were not destroyed. That the copies -- this is what it says to me -- that Alan Rodgman had were destroyed, but I would bet my life -- listen to me -- that the originals were not destroyed. He might have had copies that he had no reason

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to have.

In fact, I like the idea that you go to one central place for our research reports. It's just convenient. And you have a handle, and you know what to reproduce and when to reproduce it.

Q. Were you aware that these reports were destroyed?

A. Now, what reports?

Q. These reports by Doctor Rodgman.

A. I'm only aware if they were destroyed. I don't know whether they were or they weren't, were not original reports. He might have had copies of all these reports and more.

Q. "The follow list of formal reports were issued to Alan Rodgman and have been destroyed. Please mark your records accordingly."

A. What's your concern? I told you, I'm positive that the originals were not destroyed, and you can find out. They'll be in the file --

Q. Well, I asked Doctor Rodgman and he doesn't agree with you. The originals were destroyed --

A. I can't believe that.

Q. -- and the only way that they were preserved is the fact that no one knew they were on microfilm.

MR. DAVIS: Objection.

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MR. MARPLE: Objection to the testimony.

Q. BY MR. MCCLAIN: And that's what Doctor Rodgman said. Did you know anything about that?

MR. DAVIS: Objection.

MR. MARPLE: Objection.

A. I only know that we don't destroy reports.

Q. BY MR. MCCLAIN: Did you know that Doctor Rodgman testified here two weeks ago --

A. I wouldn't know. Of course not.

Q. -- that -- that the original reports were destroyed --

MR. MARPLE: Objection.

Q. BY MR. MCCLAIN: -- and the only way that they knew they still existed was they were found to be on microfilm, because Mr. Colby hadn't told anyone that he had microfilmed them?

MR. DAVIS: Objection.

MR. MARPLE: Objection. It's argumentative.

Q. BY MR. MCCLAIN: Are you aware of any of that?

A. No. No.

Q. Counsel hadn't talked to you about that when he asked you the question about destroying reports. Is that right?

A. I still maintain that we didn't destroy

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original reports.

Q. Then you have a disagreement with Doctor Rodgman.

A. No, I don't.

MR. MARPLE: Objection. That's argumentative.

Q. BY MR. MCCLAIN: Do you have any reason to doubt Doctor Rodgman on the subject of whether his reports were destroyed or not?

A. No. I have reason to doubt that he didn't know -- I believe he would have known that there were other copies available. He would not have destroyed them.

Q. You would defer to him on the subject.

MR. MARPLE: Objection.

A. If it was something he was concerned with.

MR. MCCLAIN: I have no further questions.

VIDEOGRAPHER: No further questions. We're off the record at 4:25.

(Witness excused at 4:25 p.m.)

(FURTHER DEPONENT SAITH NOT.)

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CERTIFICATE

State of North Carolina - County of Forsyth

I, Marion R. Ciccarelli, a court reporter, and a notary public for the state of North Carolina, do hereby certify that G. ROBERT DIMARCO, Ph.D., appeared before me on August 14, 2001, and was duly sworn by me to testify to the truth and nothing but the truth of his knowledge touching and concerning the matters in controversy in this cause; that he was thereupon examined upon his oath and his testimony reduced to typewriting under my direct supervision; that the foregoing 216 pages constitute a true and accurate record of the proceedings to the best of my knowledge and belief.

I further certify that I am neither attorney nor counsel for, nor related to nor employed by, any of the parties to the action in which this deposition was taken, and further, that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor interested, directly or indirectly, in the matters of controversy nor financially interested in the results of this action.

In witness whereof, I have hereunto set my hand and official seal on this, the 24 day of August, 2001.

Marion R. Ciccarelli

MARION R CICCARELLI

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I, *Rebecca Thomas-Coleman*, an employee of Atkinson-Baker, Inc., Court Reporters, certify that the foregoing pages 1 through 217, constitute a true and correct copy of the original deposition of [illegible] ROBERT DENMEE, PhD, taken on [illegible] 14, 2001.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Dated this 30TH day of AUGUST, 2001.

Rebecca Thomas-Coleman

REBECCA THOMAS-COLEMAN

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in

HUMPHREY

Possible Carcinogens from Tobacco

with emphasis upon

Society of Cancer Research

by

Claude E. Teague, Jr.

2 February 1953

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List of Contents

Page

2 1. Index.
2 2. General Discussion.
6 3. Special Questions.
6 a. Polynuclear Aromatic Hydrocarbons and Related Hydrocarbon Compounds.
6 b. Other Carcinogenic Agents.
9 4. Aromatic and Heterocyclic Amines.
10 5. Phenols.
10 6. Miscellaneous Agents.
10 7. Tobacco Smoke Condensate.
11 8. Tobacco Smoke Condensate and Its Fractions.
12 9. Tobacco Smoke Condensate and Its Fractions.
13 10. Tobacco Smoke Condensate and Its Fractions.
14 11. Tobacco Smoke Condensate and Its Fractions.
14 12. Tobacco Smoke Condensate and Its Fractions.
14 13. Tobacco Smoke Condensate and Its Fractions.
14 14. Tobacco Smoke Condensate and Its Fractions.

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I. OBJECT

The object of this report is to give a broad, general survey of cancer research, with emphasis on studies actually or potentially related to carcinogens from tobacco. Pertinent references are cited; where possible these are review articles with comprehensive coverage and bibliography. No attempt has been made at completeness of coverage of various topics or completeness of citation of original sources.

II. GENERAL DISCUSSION

Cancer is one of the most ancient of human diseases and its occurrence is noted in the earliest recorded history. It is one of the most universal and common of all diseases and attacks all forms of life, including plant life. In strict medical usage, "cancer" refers only to malignant tumors arising from epithelial tissue, that is, from cells contained in the skin or covering mucous or serous membranes. Malignant tumors of nonepithelial, modified, connective tissue are known medically as sarcomas, and various other names are applied to other invasive, malignant growths depending on their origins and characteristics. A medical classification of tumors, both malignant and benign, is given in Table I. To the layman, "cancer" has, through long usage, come to be an all-embracive term referring to all forms of malignant, invasive tumors, and that usage will be followed in this discussion. As used in this discussion "carcinogenic" means cancer-producing, and a "carcinogen" will mean a cancer producing agent, these being generally accepted usages.

TABLE I

Classification of Tumors

Benign	Malignant
Not invasive	Invasive
Slow growing	Rapidly growing
Do not metastasize	Metastasize
Do not interfere with health	Detrimental to health, often fatal

1. CONNECTIVE TISSUE TUMORS

   A. Benign:
      1. Fibroma, composed of fibrous tissue.
      2. Chondroma, composed of cartilage.
      3. Osteoma, composed of bone.
      4. Lipoma, composed of fat.

   B. Malignant:
      Sarcoma, a cellular tumor composed of any connective tissue cells in disorderly arrangement.

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II. MUSCLE TISSUE TUMORS --

Benign: Myoma, composed of smooth muscle tissue.

III. EPITHELIAL TUMORS

A. Benign:
1. Papillomas, composed of surface epithelium.
2. Adenomas, composed of glandular epithelium.

B. Malignant:

1. Epitheliomas, squamous epithelial cells in disorderly arrangement.
2. Carcinomas, glandular epithelial cells in disorderly arrangement.

IV. ENDOTHELIAL TUMORS

A. Benign:
1. Hemangiomas, composed of blood vessels.
2. Lymphangiomas, composed of lymph vessels.

B. Malignant:
Endotheliomas, composed of endothelial cells in disorderly arrangement.

V. PIGMENTAL TUMORS

A. Benign: Nevus, a pigmented mole.

B. Malignant: Melanoma, pigmented tumor derived from mole.

Cancer begins as a single body cell or group of cells which suddenly starts to multiply without restraint. In "spontaneous" human cancer this multiplication is initiated by unknown cause or causes. "Occupational" cancer is the result of prolonged exposure to known carcinogenic agents, as radioactive materials, x-ray, coal tar, and others. "Experimental" cancer is the result of deliberate and often, repeated, application of carcinogenic agents for the purpose of producing cancer. The unrestrained and usually rapid multiplication of cells takes place independently of the rest of the body, serving no useful bodily function, and invades the surrounding tissues or organs by direct spread. Diagnosed and treated at this stage, usually by radical surgery or radiation, the cancer may often be removed or made to subside before the entire organism is involved. Allowed to proceed unchecked, the growth spreads throughout the body. Small groups of cells break off from the primary growth and are carried by the body fluids to distant tissues where they in turn produce growths similar to the primary tumor. It is this characteristic of spread or metastasis that distinguishes a malignant from a benign tumor.

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In spite of observation, research, and theorizing for the past 2000 years, the cause of spontaneous human cancer is still unknown. By observation and by correlation of clinical data with occupation, environment, and the like, several agents causing occupational cancer have been discovered, though knowledge of how or why these agents act is very incomplete.

Early in the present century it was realized that workers in occupations involving prolonged exposure to coal tar products showed an abnormally high incidence of skin cancer. In 1915 Yamagiva and Ichikawa discovered that an experimental cancer of the skin could be produced by painting the ears of rabbits with coal tar. Detailed investigations into the nature and identity of the carcinogenic agents in coal tar indicated that the agents were probably polynuclear aromatic hydrocarbons, probably related to benzanthracene. A number of compounds related to benzanthracene were prepared and found to be carcinogenic. Concurrently, investigators working on coal tar isolated 3,4-benzpyrene, found it to be identical with synthetic 3,4-benzpyrene, and showed that both compounds had identical, positive activity. Recent work has shown that coal tar contains other potent carcinogens.

By 1930 the work of the London school under Kennaway and Cook had thoroughly established the fact that certain pure, synthetic, polynuclear aromatic compounds were true carcinogens. As a result of work of this team, together with that of the American group headed by Fieser and Bachmann, it was soon found that a large number of polycyclic aromatic hydrocarbons, together with many [illegible] derivatives, possessed carcinogenic activity. Later work showed that substances akin to polynuclear aromatic hydrocarbons but containing hetero atoms also possessed carcinogenic activity. In research activity [illegible] several other classes of compounds were found to be carcinogenic. Those receiving most attention have been the mustards, various [illegible] antimetabolites, and compounds related to 2-aminofluorene. Many other classes of compounds have been investigated and much work is currently being done on this phase of the problem.

Several methods have been used for testing of the carcinogenic effects of various substances on animals. These test methods are accurate, though rather slow. Many kinds of test animals have been used, though pure strain mice seem to be used most widely. Pure strain mice show nearly the same susceptibility to chemical carcinogenesis and are of very similar genetic constitution. Susceptibility may vary considerably from strain to strain. In one test method a dilute solution of the carcinogen in inert solvent is applied to the skin of a test animal. Application is made, usually twice weekly, for a period of several weeks. After a more or less prolonged latent period an active carcinogen gives rise to a cancerous growth of the skin. Another method involves injection of the agent subcutaneously or intraperitoneally into a test animal. The quantity injected may vary, solvent is often used, and more than one injection is sometimes made. An active carcinogen gives rise to a cancer of the connective tissue, usually at the site of injection. Many other tests have been used. Experienced technicians are able to determine within a day or two the time at which a thickening of the tissue is indicative of tumor formation. Pathological studies are used to establish whether or not a tumor was actually present.

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Carcinogens vary considerably in potency and tumors appear in treated animals only after a considerable latent period. This period varies from one to two months for very active compounds to two or more years for feebly active ones. While the test methods give very good qualitative results as to the carcinogenicity of compounds, accurate quantitative results as to relative potencies are difficult to obtain. Several systems have been devised for rating compounds as to carcinogenic activity, but none seems to be entirely satisfactory. Such systems usually take into account dosage level, dosage period, latent period, and percent of animals developing active cancers.

With the knowledge that specific, pure, organic compounds could induce experimental cancer similar in every respect to spontaneous cancer came naturally an attempt to correlate spontaneous human cancer with the presence of known chemical carcinogens. While scores of potent chemical carcinogens are now known there is no direct evidence that they are indeed responsible for spontaneous human cancer. It is possible that these chemical carcinogens may be produced in the body by abnormal processes, but substantiating evidence is lacking. To date no known chemical carcinogen has been found in cancerous tissue or in body fluids. However, such an agent may have acted as an initiator of malignancy at an earlier stage in the life of the organism, being present in unidentifiably small amounts at the time of attempted isolation. There is much current research and speculation on this phase of carcinogenesis.

It is also possible that spontaneous cancer may be caused by external carcinogenic agents, such agents entering the body with food, during respiration, or being absorbed from the body surfaces. Some such agents, as coal tar products and X-ray, have indeed been shown, by examination of clinical data, to cause an abnormally high rate of incidence of cancer (occupational type) in persons subjected to long and repeated exposure to them. Many other external agencies have been suspected and considerable research has been done and is in progress along these lines.

Several statistical studies, based on clinical data, on cancer of the respiratory system have been made, and these studies indicate an abnormal increase in the incidence of such cancers, particularly among men, during the last several decades. These studies indicate that some carcinogen, either airborn or artificially introduced into the respiratory system, is responsible for cancer of the respiratory system, and that widespread exposure to the carcinogen, particularly among men, has been fairly recent and is increasing. The present rate of increase of cancer of the respiratory system rather closely parallels the recent introduction and rate of increase of cigarette consumption, and this, together with the fact that until very recently the vast majority of cigarette smokers have been men, has raised a very considerable question. There appears to be a growing suspicion, or even acceptance, among medical men and cancer researchers that the parallel increase in cigarette consumption and incidence of cancer of the respiratory system is more than coincidence. The statistical studies continue, and their implications have become the subject of much speculation. This work is discussed in more detail in a later section.

Some workers have attempted to produce experimental cancers in test animals by application of tars obtained from tobacco, tobacco smoke, and other

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materials derived from tobacco. The results of these tests, some strongly positive and other completely negative, have been inconclusive, though would seem to indicate the presence of carcinogens. Other workers have attempted to isolate carcinogens from pyrolytic products from tobacco, and the identification of known chemical carcinogens is reported. A later section will consider this work in more detail.

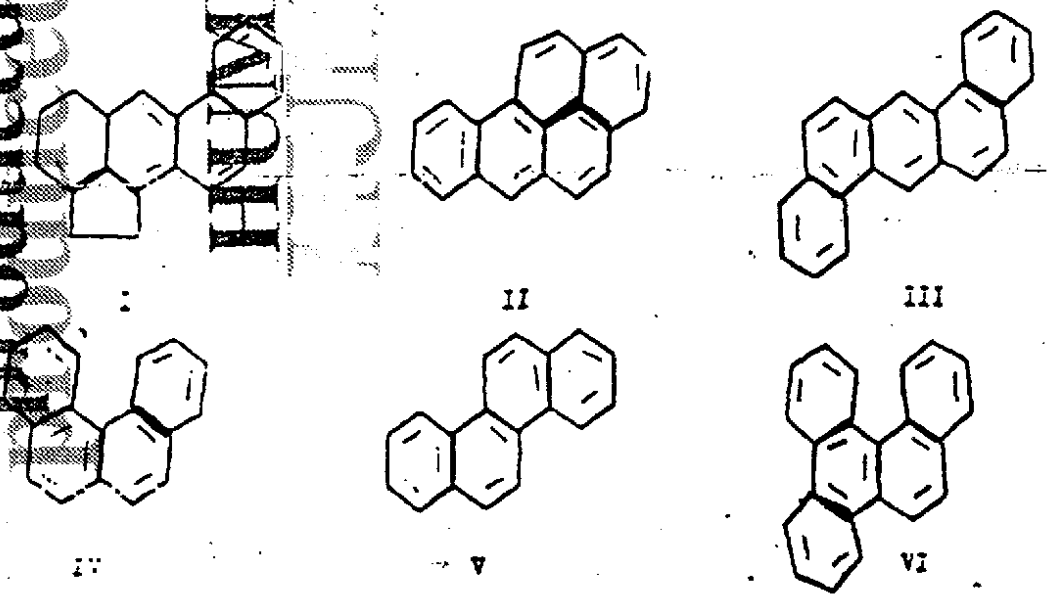
Because of the possible connection between tobacco smoking and cancer of the respiratory system it is well for manufacturers of tobacco products to be aware of past and present cancer research. Accordingly, the remaining sections of this discussion will review in some detail the present status of cancer research with particular emphasis on statistical studies relating cancer of the respiratory system to use of tobacco, and on known carcinogenic compounds and their relation to compounds present in tobacco or tobacco smoke.

III. CHEMICAL CARCINOGENS

A. Polynuclear Aromatic Hydrocarbons and Related Heterocyclic Compounds. (1 - 16)

A large number of polynuclear aromatic compounds, together with many related heterocyclic compounds, have been found to be carcinogenic. An enumeration and discussion of all such compounds is obviously beyond the scope of this discussion. Representative compounds will be considered; a very generalized correlation of activity with structure will be given.

Cholanthrene (I), 3,4-benzpyrene (II), 1,2,5,6-dibenzanthracene (III), 3,4-benzphenanthrene (IV), chrysene (V), and 1,2,3,4-dibenzphenanthrene (VI) are all carcinogens, and are representative of the basic ring structures found to accompany carcinogenic activity.



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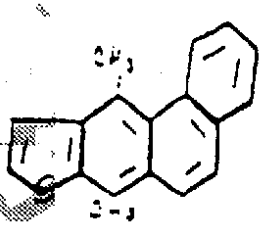
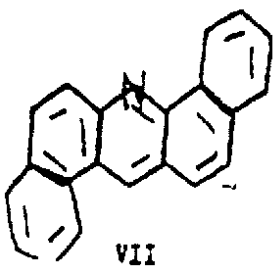
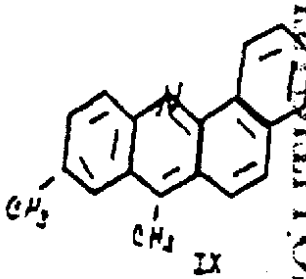
These compounds, together with their derivatives, have been studied rather extensively. A number of alkyl-, aryl-, halogeno-, cyano-, alkyloxy-, and hydroxyalkyl-derivatives of the parent hydrocarbons have proved to be active, often more active than the parent compound. Many related heterocyclic compounds have also been shown to be carcinogenic, representative examples being 4,9-dimethyl-5,6-benzthiophanthrene (VII), 1,2,5,6-dibenzacridine (VIII), and 7,9-dimethyl-3,4-benzacridine (IX).



VII



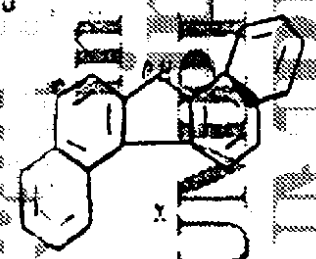
VIII



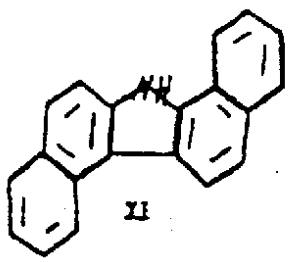
IX

Contraction of the central ring of dibenzanthracene or its isolog (VIII), as in 1,2,5,6-dibenzfluorene (X) and 1,2,5,6-dibenzcarbazole (XI), diminishes but does not abolish activity.

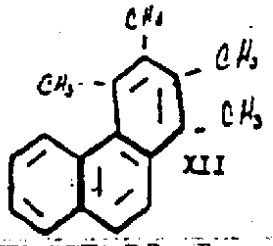
The lower limit of molecular size compatible with carcinogenic activity appears to have been reached in alkyl substituted tricyclic hydrocarbons, of which 1,2,3,4-tetramethyl phenanthrene (XII) and 9,10-dimethylanthracene (XIII) are examples.



X

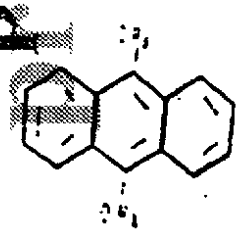


XI

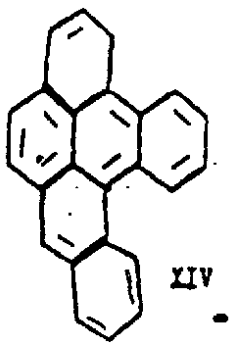


XII

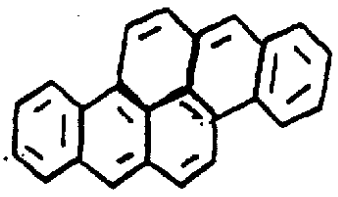
The upper limit of molecular size is still uncertain, though no compound having more than six fused rings has thus far been shown to be carcinogenic. Lying at the apparent upper limit of molecular size are benzcyclic compounds such as 1,2,3,4-dibenzopyrene (XIV) and 3,4,8,9-dibenzopyrene (XV), both extremely potent carcinogens despite their high molecular weight and insolubility.



XIII



XIV



XV

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The compounds described above serve to illustrate the important classes of carcinogenic polynuclear aromatic hydrocarbons and related compounds. Many workers have sought to correlate carcinogenic activity with structure in this class of compounds. By detailed consideration of structure versus activity in a large number of such compounds certain general conclusions have been drawn (1 - 20). Badger (10) has summarized these conclusions in an excellent review article:

1. Certain tricyclic, tetracyclic, pentacyclic and hexacyclic hydrocarbons or their homologs are cancer producing. Most of the active compounds, but not all, are derivatives of phenanthrene.

2. Many closely related heterocyclic compounds are also cancer producing. So are certain dibenzfluorenes.

3. The introduction of methyl groups into benzanthracene, benzphenanthrene, and chrysene normally leads to enhanced activity. Two methyl groups or more normally act additively. On the other hand there seems to be a limit beyond which the introduction of further methyl groups does not lead to enhanced activity. The introduction of methyl groups into the angular ring of benzanthracene does not have this effect, and all such compounds are inactive or have only trace activity.

4. Similar relationships hold for the benzacridines, except that the 1,2-benzacridines are much more carcinogenic than the 3,4-benzacridines.

5. The introduction of methyl groups in benzpyrene and dibenzanthracene series is more complex. In many cases this diminishes activity although the opposite may be true.

6. Alkyl groups other than methyl are progressively less effective as the number of carbon atoms in the chain increases.

7. Many other substituents in "favorable" positions can convert an inactive parent hydrocarbon into a carcinogenic derivative. Both electron attracting and electron repelling groups may have this property. "Favorable" positions for methyl groups are not necessarily the same for other groups.

8. Partial hydrogenation of a carcinogenic compound sometimes but not always deactivates the substance.

9. Attempts to relate carcinogenic activity with (a) shape and size of the molecule and (b) electron charge on the phenanthrene-type double bond present in most carcinogens have been only partly successful.

Studies of activity versus structure continue, and it is reasonable to suppose that with increased data and study will come a more precise understanding of the fundamental relationships.

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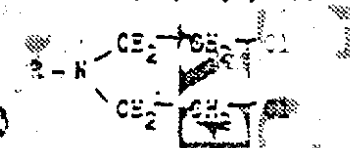
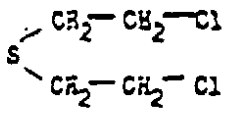
B. Other Carcinogenic Agents. (1,3,12)

The discovery that certain polynuclear aromatic compounds are carcinogenic stimulated a search for other classes of compounds which might also prove to have activity. While the polynuclear aromatic compounds have received the most attention, other structurally unrelated classes of compounds have indeed been shown to be carcinogenic. The search for other carcinogens is far from complete and continues to be actively pursued. Compounds representative of the various classes of carcinogens are listed and briefly described below.

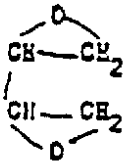
1. Aliphatic and Heterocyclic Compounds. Nitrogen mustards (XVI) and sulfur mustards (XVII) containing two active esters have been shown to be carcinogenic, apparently due to their action as cross-linking agents (21 - 24). Other substances able to cross-link acid groups by esterification and known to be carcinogenic are butadiene diepoxide (XVIII), trimethylol melamine (XII), and dimesylglycols (XX). (1, 25)



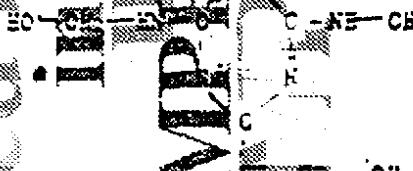
XVI



XVII



XVIII



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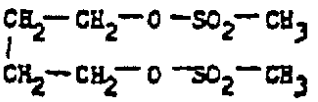
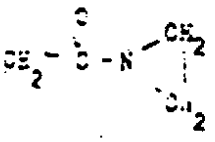
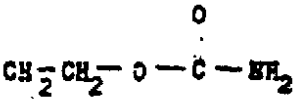


XX

Other aliphatic carcinogens are certain ethyleneimines (XXI), and urethane (XXII). (1,25)



XXI



XXII

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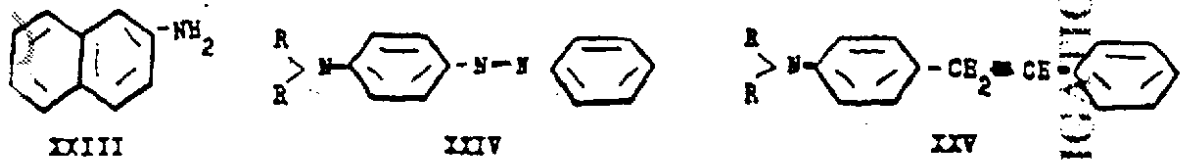
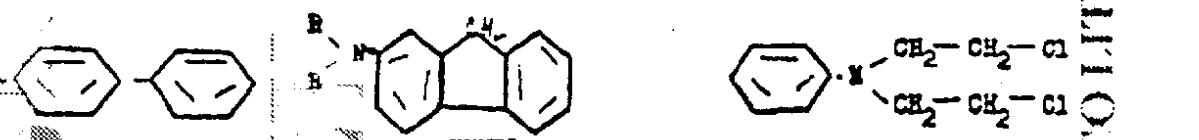
2. Aromatic Amines (1, 3) Many aromatic amines have been shown to be carcinogenic, the simplest being β-naphthalene (XXIII). Aminoazobenzenes (XXIV), aminostilbines (XXV), aminodiphenyls (XXVI), aminofluorenes (XXVII), and bis-(β-halogenoethyl)-amines (XXVIII) are representatives of this class of compounds.



XXIII XXIV XXV



XXVI XXVII XXVIII

3. Miscellaneous Agents. (1, 3) Physical carcinogenic agents include application of localised cold, implanted cellophane, and ionizing radiations, to name only a few. Numerous inorganic agents such as metallic nickel and salts of zinc and beryllium have been shown to produce cancers.

IV. TOBACCO AND CARCINOGENIC ACTIVITY

A. Statistical Studies

There is rather general agreement that the incidence of cancer of the respiratory system has increased greatly in the last half century. Several recent statistical studies have shown this marked increase and indicate a continuing rate of increase (26 - 32). Autopsy statistics throughout the world show a great increase in the incidence of cancer of the lung in relation to cancer in general (26). Whereas cancer of the lung was a rare disease 25 years ago, it now occurs nearly as often as cancer of the stomach and more often than cancer of the colon. Recent studies at several large American hospitals (26) show that it is now the most frequent visceral cancer in men in this country, while the incidence of lung cancer in females has increased appreciably, by far the greatest increase has been in males. It is estimated that the male to female incidence ratio is now about 6 to 1.

The increase in the incidence of cancer of the lung which has occurred in the present century suggests new or increased contact with carcinogenic stimuli, such stimuli being either airborne or artificially introduced into the lungs. The suggestion that smoking, and particular cigarette smoking, may be a causative factor in the induction of cancer of the respiratory system, including the oral cavity, has been made by many writers on the subject (26, 33-44). In 1941 Schraer and DeOnley (45) called attention to the similarity of the curve of increased sales of cigarettes in this country to the greater prevalence of primary cancer of the lung. They emphasized the possible etiologic relationship of cigarette smoking to this condition.

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Several recent, well-controlled, large scale, clinical studies on correlation of tobacco smoking with cancer of the lung have been made (26, 40, 41, 44). The conclusions reached by Wynder and Graham in their recent study (26) are summarized below; their survey was made by direct interview of more than 700 patients with biopsy-proven primary cancer of the lung.

1. Excessive and prolonged use of tobacco, especially cigarettes, seems to be an important factor in the induction of lung cancer.

2. The incidence of lung cancer is considerably higher among moderately heavy to chain smokers compared to the general hospital population without cancer.

3. The occurrence of lung cancer in a male nonsmoker is a rare phenomenon.

4. Tobacco seems to play a similar but somewhat less evident role in the induction of lung cancer in women. Among this group a greater percentage of nonsmokers were found than among men, with 10 to 25 being nonsmokers.

5. 96.1% of patients with cancer of the lungs who had a history of smoking had smoked for over 20 years. Few women have smoked that long and this is probably the reason for the greater present incidence among men.

6. 94.1% of the male patients with cancer of the lungs were found to be cigarette smokers, 4.0% pipe smokers, and 3.5% cigar smokers (some use more than one form of tobacco product). This prevalence of cigarette smoking is greater than among the general hospital population of the same age group. The greater practice of inhalation among cigarette smokers is believed to be a factor in the increased incidence of the disease.

7. There may be a lag of 10 years or more between the cessation of smoking and the occurrence of clinical symptoms of cancer.

8. Three independent studies have resulted in data so uniform that one may deduce the same conclusions from them.

The American Cancer Society (46) has recently initiated a very large-scale, lasting range, carefully conducted study of the relation of the smoking of tobacco products to the incidence of cancer of the respiratory system. The survey is being conducted with the help of thousands of volunteers who interview and keep detailed histories of smokers of a certain age group over an extended period. Preliminary results from this study should be available in about five years. It is expected that this study, insofar as a relationship can be proved by statistical methods, will firmly establish or disprove the relationship between tobacco smoking and cancer of the respiratory system.

B. Animal Studies with Tobacco Substances

A number of workers have made carcinogenicity tests on animals with substances derived from tobacco. The results of these tests are summarized below in tabular form.

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Year	Author	Tobacco Substance	Animal	Application	Time	Result	Reference
1900	Breech	Juice	Guina Pig	Painting	———	Proliferation	47
1911	Wacker and Schmincke	Pipe Tars	Rabbits	Injection	21 Days	Proliferation	48
1923	Schreus and Zurbelle	Purified Tar	Mice	Painting	———	Probable cancer	49
1928	Halwig	Nicotine-free ether extract of pipe tar	Mice	Painting	———	Benign ulcers	50
		400-500° Destructive distillate	Mice	Painting	———	Benign Ulcers	
1929	Lickint	Tar	Animal	———	———	Epithelial over growth	51
1930	Roffo	Smoke	Rabbit	Blowing Smoke	———	Leukoplatia	52
		Condensed Smoke in water	Rabbit	Painting	6 mos.	Carcinoma	
1931	Chiekamatsu	Tar	Rabbit	Painting	225 Days	Cancroid	53
1931	Roffo	Jet of Smoke	Rabbit	Directed at Ear	3 Years	Carcinoma	54
1931	Cooper, Lamb and Sanders	Pipe Tar	Mice	Painting	———	Carcinoma	55
1932	McNally	Tar	Rats	———	———	Too Toxic	56
		Water Soln. of Smoke	Rats	Spraying	100 Days	No effect	
1932	Roffo	Smoke	Rabbits	Directed at Ear			57

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Year	Author	Tobacco	Animal	Application	Time	Result	Reference
1932	Bogen and Loomis	Tar from Dust	Mice	Painting	1 Year	No Effect	58
1934	Lu-Fu-Ku	Tar from Smoke	Rabbit	Painting	148-182 Days	Cancer	59
1935	Schurch and Winterstein	Cigar Tar	———	———	———	No Activity	60
1936	Roffo	Pills of Tar	Rats	Implant	8 Mos.	Tumors	61
1937	Schurch and Winterstein	Tar from Cigar Smoke	Rabbits	Paint	48 Mos.	Carcinoma	62
1937	Tahi	Tar	Mice	Paint	———	Cancer	63
1939	Campbell	Smoke Tar	Mice	Paint	10 Mos.	Carcinoma	64
1939	Roffo	Dest. Distillate	Rabbits	Paint	———	Cancer	65
1939	Roffo	Dest. Distillate	Rabbits	Paint	9-10	Cancer	66
1940	Roffo	Extracted Tars	———	———	———	Carcinoma	67
		Pyrolytic Tars	Rabbits	———	———	Carcinoma	
1941	Flory	Pyrolytic Tars	Rabbits	Paint	238-600 Days	Papillomas Carcinomatod tumors	68
1941	Martens	Cigarette Smoke	Mice	Exposure		Metaplasia, Ulcers	69
1941	Roffo	Tar	Rats	Painting	330 Mos.	Metric Lesions	70
1942	Roffo	Pyrolytic Tars	Rabbits	Paint	———	Carcinomas	71

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Many of the original articles appear in publications that are not readily available; in those cases information has been obtained from abstracts or other references to the original work. Often the source and method of preparation of the tobacco substance is vague, and often no dosage or incidence data are given. Also, a variety of test animals, differing in susceptibility to carcinoma, have been used. Various workers have used various criteria for classifying the tumorous growths produced, and no piece of work is directly comparable to any other work. In the above table where the tests produced one or more cancerous growths the test series was considered as positive and the result is tabulated as cancer, or like term. The positive results are considered to be more significant than the negative ones.

Bearing in mind the above qualifying statements, certain general conclusions may be drawn from the data presented. In all but a few cases one or more tumors, usually of a malignant type, resulted from application of various tobacco substances to the skins of a variety of test animals. In most cases the tumors appeared only after a more or less prolonged latent period. The results are somewhat inconclusive but indicate that substances derived from tobacco have some degree of carcinogenic activity.

C. Carcinogens Identified in Tobacco Substances.

Very little work on isolation and characterization of carcinogens from tobacco substances has been reported in the literature. Hoffe (72) in 1937 reported that hydrocarbons with condensed benzene nuclei were present in materials obtained by direct distillation of many varieties of tobaccos at temperatures ranging from 85° to 350°C. His report was based on spectroscopic data. In 1939 Hoffe (73) reported that a product was obtained from a certain cancer producing tobacco tar by distillation that had the spectrographic qualities of benzpyrene (II), and stated that the product was a potent carcinogen. In 1939 Hoffe (74) described a destructive distillation where fractions were obtained at 100-120°, and at 350°C. The low boiling fraction showed no carcinogenic activity. The high boiling fraction was reported to contain anthracene, phenanthrene, and benzpyrene; this fraction was strongly carcinogenic giving a 96% incidence of cancer when painted on the skin of rabbits. The residue contained condensed benzene nuclei and was strongly carcinogenic although less so than the high boiling distillate. The spectra of tars from 9 different varieties of tobacco were all similar to that of phenanthrene. In 1941 Hoffe (75) reported isolation of a benzpyrene from a pyrolytic distillate of tobacco. The benzpyrene was highly carcinogenic in animal tests.

The original articles referred to above were not readily available; most of the information given was obtained from abstracts and other references to the original work. On the basis of the information at hand it would appear that polynuclear aromatic compounds occur in the pyrolytic products of tobacco. Benzpyrene and "a benzpyrene", both carcinogens, were identified in the distillates. Though Hoffe appears to be well known and widely recognized as an authority in the field of cancer research, it is perhaps unwise to draw sweeping conclusions from the unsupported work of one man. More work is needed in this particular field before final conclusions should be drawn.

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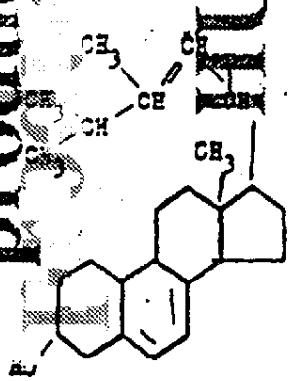
D. Compounds Isolated from Tobacco Substances and the Possibility of Carcinogens Arising from Them.

Aside from the polynuclear hydrocarbons discussed above, no other compounds having known or suspected carcinogenic activity have been isolated from tobacco substances. This does not necessarily mean that such compounds are not present. Tobacco contains a large number of organic compounds and many remain to be isolated and characterized. From the standpoint of carcinogenic activity of tobacco the important fact to be determined is whether or not carcinogens, if present or produced, are present in tobacco smoke after it leaves the cigarette.

Even if carcinogens do not occur in tobacco it is possible that carcinogenic substances may be formed during the smoking process. During smoking, tobacco, containing scores of organic compounds, is subjected to a pyrolytic or destructive distillation process at elevated temperatures. Oxidation, hydrolysis, and other reactions may take place at the same time. Carcinogenic substances have been formed by similar processes at similar temperatures. Extracts of soot are carcinogenic. Tars from acetylene heated at 700°C. and isoprene heated to 720°C. were carcinogenic (76). At higher temperatures destructive distillates of petroleum, human skin, yeast, cholesterol, turpentine, rice polishings, and crude sugar were all shown to be carcinogenic, as were heated animal and vegetable fats (68).

Of the above materials, acetylene, and compounds similar to cholesterol, are present in tobacco or tobacco smoke. Phytosterols, sterols similar to cholesterol, have been found in tobacco (77, 78) and Roffo (77) has reported that their removal prior to pyrolysis distinctly lowers the carcinogenic activity of the pyrolysate. On examination of the structure of ergosterol (XIV), a typical phytosterol, certain similarities to the structure of cholanthrene (I), a potent carcinogen, are evident. Aromatization of sterols, steroids, and like substances by the body has been offered as a possible explanation of the origin of spontaneous human cancer. Pyrolysis of cholesterol produces carcinogenic substances related to cholanthrene (I). It is reasonable to assume, particularly in light of the work of Roffo, that plant sterols known to be present in tobacco might give similar pyrolytic products.



Pyrolysis → I (Shown on page 6)

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Under pyrolytic conditions acetylene and various other unsaturates may polymerize and cyclize to give aromatic rings. This behavior is well known. Such compounds have been found in tobacco and tobacco smoke and the possibility exists that they may be converted to polynuclear aromatic hydrocarbons.

A number of nitrogen heterocycles, the alkaloids, are present in tobacco. By condensation and cyclization of side chains during pyrolysis such compounds might give rise to derivatives of benzacridine (VII), or dibenzcarbazole (XI).

Pyrolysis of a simple organic compound is often a complex reaction, and attempts to postulate pyrolytic products arising from a mixture containing countless organic compounds borders upon pure speculation. The above suggestions merely represent some of the possibilities that exist.

B. Tobacco Additives

In the manufacture of tobacco products a number of organic materials are added to the leaf tobacco. Such additives are flavorants, humectants, and like substances. It is possible that one or more of these materials may give rise to carcinogenic substances. The writer does not have access to information as to the additives used and is therefore unable to evaluate them.

Cigarettes are encased in paper, an organic material which could possibly burn or pyrolyze to give carcinogens. The same applies to the glue and ink used on the paper.

V. CONCLUSIONS

The increased incidence of cancer of the lung in man which has occurred during the last half century is probably due to new or increased contact with carcinogenic stimuli. The closely parallel increase in cigarette smoking has led to the suspicion that tobacco smoking is an important etiologic factor in the induction of primary cancer of the lung. Studies of clinical data tend to confirm the relationship between heavy and prolonged tobacco smoking and incidence of cancer of the lung. Extensive though inconclusive testing of tobacco substances on animals indicates the probable presence of carcinogenic agents in these substances. One worker has identified known carcinogens in a tobacco pyrolysate. Compounds are present in tobacco which on pyrolysis could theoretically give rise to compounds similar to known carcinogens. The possible role of tobacco additives and cigarette paper in the production of carcinogens cannot be determined because of lack of access to information on substances used.

VI. RECOMMENDATIONS

A. It is recommended that this preliminary, broad survey of cancer research be supplemented by complete, detailed surveys of the individual topics discussed above. Such surveys should be made at frequent and regular intervals in the future so as to make current developments promptly available to interested persons.

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b. In line with the above, it is recommended that the Research Library subscribe to journals covering the field of cancer research. A file of pamphlets and reprints, together with pertinent books, reports, and the like, should be assembled.

c. It is recommended that all tobacco additives, i.e. flavorants and humectants, used by this company be examined carefully with respect to their possible role as carcinogens or carcinogens producing agents.

2. In view of the facts presented in this report it is recommended that management take cognizance of the problem and its implications to our industry, and that positive research action be planned and initiated without delay.

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4. Study, design and evaluate new or improved systems for delivery of nicotine which will provide the minimum satisfying amount of nicotine in attractive form, free of allegedly harmful combustion products.
5. Study means for enhancing nicotine satisfaction via synergists, alteration of pH, or other means, to minimize dose level and maximize desired effects.
6. Monitor developments in materials and products which may compete with nicotine products or which might be combined with nicotine products to provide added advantages or satisfactions.
7. Monitor work by others which might be aimed at improved nicotine delivery systems of the type proposed here.
8. Search for and evaluate other physiologically active components of tobacco or its smoke which may provide desired effects to the smoker.

Claude E. Teague, Jr.
April 14, 1972

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RESEARCH PLANNING MEMORANDUM

ON

THE NATURE OF THE TOBACCO BUSINESS AND THE CRUCIAL ROLE OF NICOTINE THEREIN

PLAINTIFF'S DEPOSITION EXHIBIT 8

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MEMORANDUM:

In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry. Tobacco products, uniquely, contain and deliver nicotine, a potent drug with a variety of physiological effects. Related alkaloids, and probably other compounds, with desired physiological effects are also present in tobacco and/or its smoke. Nicotine is known to be a habit-forming alkaloid, hence the confirmed user of tobacco products is primarily seeking the physiological "satisfaction" derived from nicotine -- and perhaps other active compounds. His choice of product and pattern of usage are primarily determined by his individual nicotine dosage requirements and secondarily by a variety of other considerations including flavor and irritancy of the product, social patterns and needs, physical and manipulative gratifications, convenience, cost, health considerations, and the like. Thus a tobacco product is, in essence, a vehicle for delivery of nicotine, designed to deliver the nicotine in a generally acceptable and attractive form. Our Industry is then based upon design, manufacture and sale of attractive dosage forms of nicotine, and our Company's position in our Industry is determined by our ability to produce dosage forms of nicotine which have more overall value, tangible or intangible, to the consumer than those of our competitors.

The habituated user of tobacco products is said to derive "satisfaction" from nicotine. Although much studied, the physiological actions of nicotine are still poorly understood and appear to be many and varied. For example, in different situations and at different dose levels, nicotine appears to act as a stimulant, depressant, tranquilizer, psychic energizer, appetite reducer, anti-fatigue agent, or energizer, to name but a few of the varied and often

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contradictory effects attributed to it. Many of these same effects may be achieved with other physiologically active materials such as caffeine, alcohol, tranquilizers, sedatives, euphorics, and the like. Therefore, in addition to competing with products of the tobacco industry, our products may, in a sense, compete with a variety of other products with certain types of drug action. All of these products, tobacco and other, appear to have certain common attributes in that they are used largely to relieve, in one way or another, the fatigues and stresses which arise in the course of existence in a complex society.

Happily for the tobacco industry, nicotine is both habituating and unique in its variety of physiological actions, hence no other active material nor combination of materials provides equivalent "satisfaction". Whether nicotine will, over the long term, maintain its unique position is subject to some reasonable doubt. With increased sophistication of knowledge in the biological and pharmaceutical areas, a superior or at least equivalent product or product mixture may emerge. For this reason, it would be a mistake to assume that the tobacco industry, as we now know it, is immortal or that no direct competition from organizations outside of the tobacco industry will ever occur. It is safe to assume, however, that nicotine will retain its unique position throughout the present ten year planning period, and probably for a much longer span of time.

If nicotine is the sine qua non of tobacco products and tobacco products are recognized as being attractive dosage forms of nicotine, then it is logical to design our products -- and where possible, our advertising -- around nicotine delivery rather than "tar" delivery or flavor. To do this we need to

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develop new data on such things as the physiological effects of nicotine, the rate of absorption and elimination of nicotine delivered in different doses at different frequencies and by different routes, and ways of enhancing or diminishing nicotine effects and "satisfactions". In the absence of such data, we may survey the market and conclude that current cigarette products delivering about 1.3 mg. of nicotine appear to "satisfy" the typical smoker. This, somewhat crudely, establishes a target dosage level for design of new products. An accompanying Research Planning Proposal describes that approach in some detail. However, if we knew more about nicotine absorption, action, elimination, enhancement and the like, it should, in theory, be possible to more precisely specify, and deliver, the optimum amounts of nicotine activity in sophisticated products which would be more satisfying and desirable to the user. This area merits consideration and activity.

Before proceeding too far in the direction of design of dosage forms for nicotine, it may be well to consider another aspect of our business; that is, the factors which induce a pre-smoker or non-smoker to become a habituated smoker. Paradoxically, the things which keep a confirmed smoker habituated and "satisfied", i.e., nicotine and secondary physical and manipulative gratifications, are unknown and/or largely unexplained to the non-smoker. He does not start smoking to obtain undefined physiological gratifications or reliefs, and certainly he does not start to smoke to satisfy a non-existent craving for nicotine. Rather, he appears to start to smoke for purely psychological reasons -- to emulate a valued image, to conform, to experiment, to defy, to be daring, to have something to do with his hands, and the like. Only after experiencing smoking for some period of time do the physiological "satisfactions" and habituation become apparent and needed. Indeed, the first

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smoking experiences are often unpleasant until a tolerance for nicotine has been developed. This leaves us, then, in the position of attempting to design and promote the same product to two different types of market with two different sets of motivations, needs and expectations. The same situation is encountered in some industries, but the problem is usually not as severe.

If what we have said about the habituated smoker is true, then products designed for him should emphasize nicotine, nicotine delivery efficiency, nicotine satisfaction, and the like. What we should really make and sell would be the proper dosage form of nicotine with as many other built-in attractions and gratifications as possible -- that is, an efficient nicotine delivery system with satisfactory flavor, mildness, convenience, cost, etc. On the other hand, if we are to attract the non-smoker or pre-smoker, there is nothing in this type of product that he would currently understand or desire. We have deliberately played down the role of nicotine, hence the non-smoker has little or no knowledge of what satisfactions it may offer him, and no desire to try it. Instead, we somehow must convince him with wholly irrational reasons that he should try smoking, in the hope that he will for himself then discover the real "satisfactions" obtainable. And, of course, in the present advertising climate, our opportunities to talk to the pre-smoker are increasingly limited, and therefore, increasingly ineffective. Would it not be better, in the long run, to identify in our own minds and in the minds of our customers what we are really selling, i.e., nicotine satisfaction? This would enable us to speak directly of the virtues of our product to the confirmed smoker, and would educate the pre-smoker, perhaps indirectly but effectively, in what we have to offer and what it would be expected to do

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But again, the picture is not quite all that clear. Critics of tobacco products increasingly allege that smoking is dangerous to the health of the smoker. Part of this alleged danger is claimed to arise from ingestion of nicotine and part is claimed to arise from smoke components or smoke "tar". If, as proposed above, nicotine is the sine qua non of smoking, and if we meekly accept the allegations of our critics and move toward reduction or elimination of nicotine from our products, then we shall eventually liquidate our business. If we intend to remain in business and our business is the manufacture and sale of dosage forms of nicotine, then at some point we must make a stand. We should know more, rather than less, than our critics about the physiological effects of nicotine, and we should in all ways scientifically validate and speak to the beneficial effects and "satisfactions" derived from use of nicotine. Essentially all commercial drugs give rise to some undesirable side effects, but we continue to use them with great benefit to humanity because of their overriding beneficial effects. Might we not take a leaf from that book in our approach to nicotine? Unless we do, our long-term prospects become unattractive.

Our critics have lumped "tar" and nicotine together in their allegations about health hazards, perhaps because "tar" and nicotine are generated together in varying proportions when tobacco is smoked. An accompanying Research Planning Memorandum suggests an approach to reducing the amount of "tar" in cigarette smoke per unit of nicotine. That is probably the most realistic approach in today's market for conventional cigarette products. However, another more futuristic approach is possible which goes more directly to the fundamentals of the alleged problem.

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If our business is fundamentally that of supplying nicotine in useful dosage form, why is it really necessary that allegedly harmful "tar" accompany that nicotine? There should be some simpler, "cleaner", more efficient and direct way to provide the desired nicotine dosage than the present system involving combustion of tobacco or even chewing of tobacco. A conventional 1000 mg. tobacco rod containing about 20 mg. of nicotine is smoked to produce only about 1.3 mg of smoke nicotine, accompanied by about 20 mg. of "tar" and 20 mg. of gas phase matter; and a ~~substantial~~ part of the 1.3 mg of smoke nicotine is lost to the smoker via exhaled smoke -- surely an inefficient nicotine delivery system. It should be possible to obtain pure nicotine by synthesis or from high-nicotine tobacco. It should then be possible, using modifications of techniques developed by the pharmaceutical and other industries, to deliver that nicotine to the user in efficient, effective, attractive dosage form, accompanied by no "tar", gas phase, or other allegedly harmful substances. The dosage form could incorporate various flavorants, enhancers, and like desirable additives, and would be designed to deliver the minimum effective amount of nicotine at the desired release rate to supply the "satisfaction" desired by the user. Such a product would maximize the benefits derived from nicotine, minimize allegedly undesirable over-dosage side effects from nicotine, and eliminate exposure to other materials alleged to be harmful to the user. For the long term, we should be working toward development of such products -- if we do not, inevitably someone else will, and there are strong indications that others are already moving in this direction.

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In the present real situation, where nothing has been done to counteract the adverse allegations about nicotine and where conventional products delivering adequate amounts of nicotine dominate the marketplace, no abrupt change in our posture or strategy would be appropriate or reasonable. The approaches advocated above are aimed at stopping and eventually reversing a trend that may in the long term put us out of business, and are intended to lay a framework of philosophy around which research efforts may now begin. Hopefully, some day we will rejoice rather than despair when a new crop of tobacco shows an unusually high content of nicotine, our primary product. Hopefully, with time we will be able to develop sophisticated and improved minimum dosage forms for nicotine which will be more satisfying to the user and free of alleged health hazards. And hopefully, by that time, we will have been able to establish and use information showing that use of nicotine fills real, demonstrable human needs, the beneficial effects overriding the alleged harmful side effects.

INDICATED RESEARCH DEPARTMENT ACTIVITIES AND APPROACHES:

If the above is a valid line of reasoning, then our long-term future courses of action should be as follow:

1. Recognize the key role of nicotine in consumer satisfaction, and design and promote our products with this in mind.
2. More precisely define the minimum amount of nicotine required for "satisfaction" in terms of dose levels, dose frequency, dosage form, and the like. This would involve biological and other experiments.
3. Sponsor in-depth studies of the physiological, psychological and other effects of nicotine, aimed at demonstrating the beneficial effects of nicotine and at disproving allegations that nicotine

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4. Study, design and evaluate new or improved systems for delivery of nicotine which will provide the minimum satisfying amount of nicotine in attractive form, free of allegedly harmful combustion products.
5. Study means for enhancing nicotine satisfaction via synergists, alteration of pH, or other means, to minimize dose level and maximize desired effects.
6. Monitor developments in materials and products which may compete with nicotine products or which might be combined with nicotine products to provide added advantages or satisfactions.
7. Monitor work by others which might be aimed at improved nicotine delivery systems of the type proposed here.
8. Search for and evaluate other physiologically active components of tobacco or its smoke which may provide desired effects to the smoker.

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PLAINTIFF'S DEPOSITION EXHIBIT 3

RESEARCH PLANNING MEMORANDUM

ON

SOME THOUGHTS ABOUT NEW BRANDS OF CIGARETTES FOR THE YOUTH MARKET

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D R A F T

SOME THOUGHTS ABOUT NEW BRANDS OF CIGARETTES
FOR THE YOUTH MARKET

At the outset it should be said that we are presently, and I believe unfairly, constrained from directly promoting cigarettes to the youth market: that is, to those in the approximately twenty-one year old and under group. Statistics show, however, that large, perhaps even increasing, numbers in that group are becoming smokers each year, despite bans on promotion of cigarettes to them. If this be so, there is certainly nothing immoral or unethical about our Company attempting to attract those smokers to our products. We should not in any way influence non-smokers to start smoking; rather we should simply recognize that many or most of the "21 and under" group will inevitably become smokers, and offer them an opportunity to use our brands.

Realistically, if our Company is to survive and prosper, over the long term, we must get our share of the youth market. In my opinion this will require new brands tailored to the youth market; I believe it unrealistic to expect that existing brands identified with an over-thirty "establishment" market can ever become the "in" products with the youth group. Thus we need new brands designed to be particularly attractive to the young smoker, while ideally at the same time being appealing to all smokers.

Several things will go to make up any such new "youth" brands, the most important of which may be the image and quality - which are, of course, interrelated. The questions then are: What image? and What quality? Perhaps these questions may best be approached by consideration of factors influencing pre-smokers to try smoking, learn to smoke and become confirmed smokers.

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Table I attempts to define some of the more important effects expected or derived from cigarette smoking by pre-smokers, "learning" smokers and confirmed smokers. If this incomplete, subjective, simplistic analysis is even approximately correct, there are sharp, perhaps exploitable, differences between pre-smokers, "learners" and confirmed smokers in terms of what they expect or derive from smoking. Let us examine these differences.

For the pre-smoker and "learner" the physical effects of smoking are largely unknown, unneeded, or actually quite unpleasant or awkward. The expected or derived psychological effects are largely responsible for influencing the pre-smoker to try smoking, and provide sufficient motivation during the "learning" period to keep the "learner" going, despite the physical unpleasantness and awkwardness of the period.

In contrast, once the "learning" period is over, the physical effects become of overriding importance and desirability to the confirmed smoker, and the psychological effects, except the tension-relieving effect, largely wane in importance or disappear.

The common thread binding the three groups together appears to be the fact that smoking of cigarettes offers and provides a desired mechanism for coping with the stresses of living, which may range from boredom to high tension and from fatigue to high arousal and hyperactivity. Once this mechanism has been experienced and used, physical and psychological habit patterns are firmly established and become self-perpetuating.

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TABLE I

EFFECTS EXPECTED OR DERIVED FROM CIGARETTE SMOKING

	Pre-Smoker[1]	Learner[1]	Smoker[1]
I. PHYSICAL EFFECTS			
A. Nicotine Response	0	--	+++
B. Sensory Effects			
1. Irritancy-Harshness	0	---	-
2. Flavor	+	-	+
3. Other Mouth Feel - Dryness, Astringency, etc.	0	--	-
4. Visual - Pack, cigarette and smoke attributes	0	+	++
C. Manipulative Effects - Handling, lighting, puffing, holding, ashing, extinguishing	-	-	++
II. PSYCHOLOGICAL EFFECTS			
A. Group Identification - Participating, sharing, conforming, etc.	+++	+++	0
B. Stress and Boredom Relief - Buys time, valid interruption, bridges awkward times and situations, something to do, etc.	+	++	+++
C. Self-Image Enhancement - Identification with valued persons, daring, sophisticated, free to choose, adult, etc.	++	+++	-
D. Experimentation - Try something new, experiment, etc.	+++	+++	0

[1] + = positive
0 = none
- = negative

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If the above analysis is approximately correct, then the basic theme for promoting any cigarette to any group should aim, directly or indirectly, at the desirability of using a given brand as a mechanism for coping with stress. Brands tailored for the beginning smoker should emphasize the desirable psychological effects of smoking, also suggesting the desirable physical effects to be expected later. Happily, then, it should be possible to aim a cigarette promotion at the beginning smoker, at the same time making it attractive to the confirmed smoker. The information and outline in Table I then may be used as a basis for arriving at some specifications for new "youth" brands and for determining how they should be promoted.

1. PHYSICAL EFFECTS

Having identified these as highly desirable to the confirmed smoker but largely unknown, unpleasant, awkward and/or undesirable to the pre-smoker or "learner", the effort here should be to affect a compromise to minimize the undesirable effects while retaining these which later become desirable.

A. Nicotine Effects - Nicotine should be delivered at about 1.0-1.3 mg./cigarette, the minimum for confirmed smokers. The rate of absorption of nicotine should be kept low by holding pH down, probably below 6.

B. Sensory Effects

1. Irritancy-Harshness - The beginning smoker and inhaler has a low tolerance for smoke irritation, hence the smoke should be as bland as possible.

2. Flavor - The flavor of tobacco smoke is initially foreign, and not pleasant. One cultivates a taste for smoke much as one learns to like olives or dry wines. Perhaps, as in the case of taste of water, there is no really "good" flavor, only degrees of "bad" flavor. Thus for the beginning smoker the cigarette smoke should have a

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moderate level of blended tobacco flavor, but should be as free as possible from strong, unpleasant flavors such as stemmy flavor, etc. A "tar" delivery of 12-14 mg/cigarette should provide the desired flavor level.

3. Other Mouth Feel - The smoke should be "bland" with respect to astringency, hotness, dryness and the like. Again, the theory is that any mouth effect is new and different, hence should be as bland and free of obvious negatives as possible.

4. Visual - The package and cigarette should be pleasing to the eye, as will be discussed further below. The amount and density of exhaled smoke should be such as to be clearly visible and not thin or scanty. A tar level of 10-14 mg/cigarette should meet this requirement.

C. Manipulative Effects - Carrying, opening and using the package should be convenient. The cigarette should be as long as possible, probably 100 mm, to facilitate lighting. The rod should be reasonably firm, and a moderately soft, round filter tip should be used. The draft resistance prior to and during smoking should be as low as practical and should not exceed VANTAGE specifications. The product should require, thus, minimum effort and care to handle and use.

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II. PSYCHOLOGICAL EFFECTS

These are the expected or derived gratifications which influence a pre-smoker to try smoking and which sustain the beginning smoker during the largely physically awkward and unpleasant "learning to smoke" phase. These effects also largely determine which brand the pre-smoker will experiment and learn with.

A. Group Identification - Pre-smokers learn to smoke to identify with and participate in shared experiences of a group of associates. If the majority of ones closest associates smoke cigarettes, then there is strong psychological pressure, particularly on the young person, to identify with the group, follow the crowd, and avoid being out of phase with the group's value system even though, paradoxically, the group value system may esteem individuality. This provides a large incentive to begin smoking. If this be true, then the same effect strongly influences the brand chosen, it likely being the popular, "in" brand used by ones close associates.

Thus a new brand aimed at the young smoker must somehow become the "in" brand and its promotion should emphasize togetherness, belonging and group acceptance, while at the same time emphasizing individuality and "doing ones own thing."

B. Stress and Boredom Relief - The teens and early twenties are periods of intense psychological stress, restlessness and boredom. Many socially awkward situations are encountered. The minute or two required to stop and light a cigarette, ask for a light, find an ash tray, and the like provide something to do during periods of awkwardness or boredom, and afford a little "time-out period" when confronting a stressful situation. Smoking also gives one something to do with the hands, eyes, etc. and something to talk about in a situation where otherwise one might simply have nothing to do or say.

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This desirable attribute of smoking should be strongly emphasized in promoting a new youth brand.

C. Self-Image Enhancement - The fragile, developing self-image of the young person needs all of the support and enhancement it can get. Smoking may appear to enhance that self-image in a variety of ways. If one values, for example, an adventurous, sophisticated, adult image, smoking may enhance ones self-image. If one values certain characteristics in specific individuals or types and those persons or types smoke, then if one also smokes he is psychologically a little more like the valued image. This self-image enhancement effect has traditionally been a strong promotional theme for cigarette brands and should continue to be emphasized.

D. Experimentation - There is a strong drive in most people, particularly the young, to try new things and experiences. This drive no doubt leads many pre-smokers to experiment with smoking, simply because it is there and they want to know more about it. A new brand offering something novel and different is likely to attract experimenters, young and old, and if it offers an advantage it is likely to retain these users.

There is another psychological factor which did not readily fall into Table I, but which may be quite important. That category might be called "Anti-Establishment Attitudes". It does not enter into the decision to start smoking but may strongly influence the brand chosen. Today more than ever, young people tend to reject whatever is accepted by the "over-thirty" establishment, which includes their parents. If "Brand 30" is the accepted "in" brand with the establishment, it is likely that many young smokers will

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almost automatically reject that brand and start with something else. They will more likely start with "Brand 20+" which is both the "in" thing with their closest age group and the "out" thing with the "over-thirty" group. Probably in todays market, WINSTON is the "Brand 30+" and Marlboro is the "Brand 20+". Happily, the Marlboro will eventually age out of its "in" position with youth, as WINSTON appears to have already done. Now is the time to launch the next brand to become the "in" cigarette with the next generation as Marlboro ages from "in" to, hopefully "out and over-thirty" status, hence becomes something for youth to avoid.

A final psychological factor which also did not fall readily into Table I involves smoking-health attitudes. The smoking-health controversy does not appear important to the group because, psychologically, at eighteen, one is immortal. Further, if the desire to be daring is part of the motivation to start smoking, the alleged risk of smoking may actually make smoking attractive. Finally, if the "older" establishment is preaching against smoking, the anti-establishment sentiment discussed above would cause the young to want to be defiant and smoke. Thus, a new brand aimed at the young group should not in any way be promoted as a "health" brand, and perhaps should carry some implied risk In this sense the warning label on the package may be a plus.

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We have looked, at some length, at what qualities and image a new brand aimed at the youth market should have. At this point, it will be useful to summarize what has been said; in admittedly general terms:

Product Quality Factors

1. Moderate level of nicotine (1.0-1.3 mg/cigarette) delivered at pH (5.8-6.0) to insure slow absorption.
2. Moderate level of blended tobacco flavor ("tar" of 12-14) free of undesirable (e.g. stemmy) flavors.
3. Bland, soft, moist mouth-feel, with minimal irritancy, harshness, astringency, possibly very lightly mentholated.
4. In "standard" range of diameter and firmness, with resilient filter or mouthpiece, probably 100 mm in length.
5. Different package type or packaging material, perhaps containing fewer cigarettes, therefore less bulky.
6. Some visible novelty or difference in product or package to set apart from conventional cigarettes, ideally in direction of greater manipulative convenience for beginning smoker.

Product Image Factors

1. Should emphasize participation, togetherness, and membership in a group, one of the group's primary values being individuality.
2. Should be strongly perceived as a mechanism for relieving stress, tension, awkwardness, boredom, and the like.
3. Should be associated with doing one's own thing to be adventurous, different, adult, or whatever else is individually valued.
4. Should be perceived as some sort of new experience, something arousing some curiosity, and some challenge.
5. Should be different from established brands used by the over-thirty and perhaps even over-twenty-five groups. Must become the proprietary "in" thing of the "young" group.
6. Should not be perceived as a "health" brand.

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The enumerated Product Quality Factors should be easy to achieve, except those requiring some ill-defined novelty. The Product Image Factors, of course, describe a promotional approach, and it is most likely that the name and appearance of the product will here become crucial in establishing the desired image. The name may be the most important factor, determining the appearance of the package and summarizing the image to be promoted.

Ideally, the name chosen should have a double meaning; that is, one desirable connotation in "straight" language and another in the jargon of youth. A current example may be Kool, which reads on "cool" cat in youth jargon, and also literally connotes a refreshing physical sensation. Another way of approaching the name or image would be to choose one which evokes different but desirable responses from different age groups. Thus the Marlboro western theme suggests independence, clean air, open spaces and freedom to the youth group, while at the same time suggesting the "good old days", hard work, white hats over black hats, and the like to the older generation. In passing, it is interesting to note that Marlboro is a distinguished, dignified British name, and there is a certain inconsistency in equating this image with the West.

A careful study of the current youth jargon, together with a review of currently used high school American history books and like sources for valued things might be a good start at finding a good brand name and image theme. This is obviously a task for marketing people, not research people.

Assuming that at some point marketing people will establish a name and image for a new youth brand, and assuming that the thoughts on product quality factors expressed above are approximately correct, then Research and TPD should be able to provide the product needed. Most of the product specifications defined are achievable with present technology. Those which require new technology would appear to be: (1) control of irritancy and related mouth-feel factors to produce a bland

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smoke, and (2) creation of some useful, demonstrable novelty in filter, mouthpiece, package or other aspect of the product system.

Our Company needs to take advantage of the opportunity to market new youth brands of cigarettes. The thoughts expressed here may provide a preliminary agenda for discussions between Research, TPD, Marketing and Management, aimed at more precisely defining what we could ultimately make and promote. It is hoped that such discussions will soon ensue. Meanwhile, it becomes appropriate for Research to seek ways to control smoke irritancy and to seek to create novel, useful cigarette systems.

Claude E. Teague, Jr.
February 2, 1973

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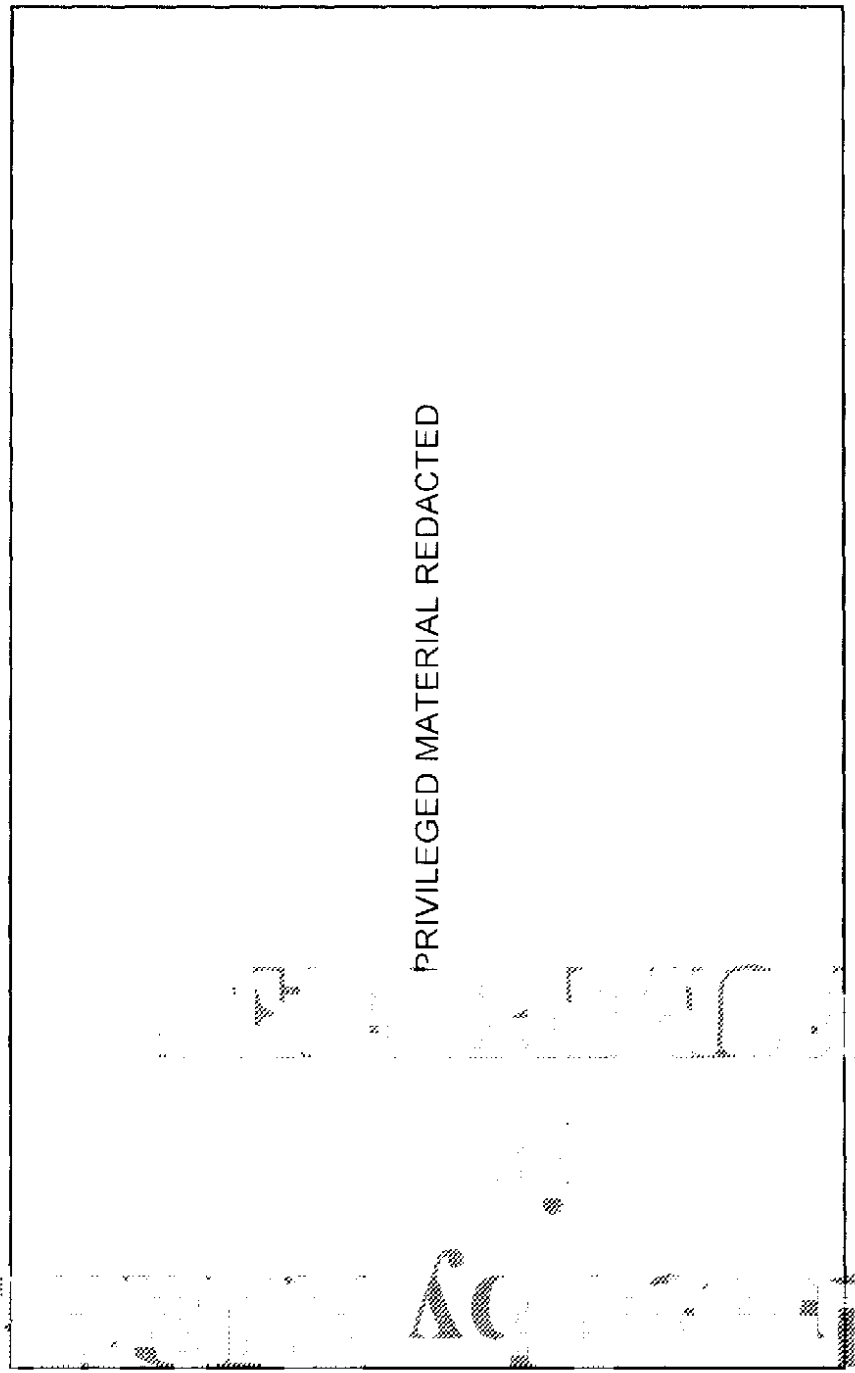

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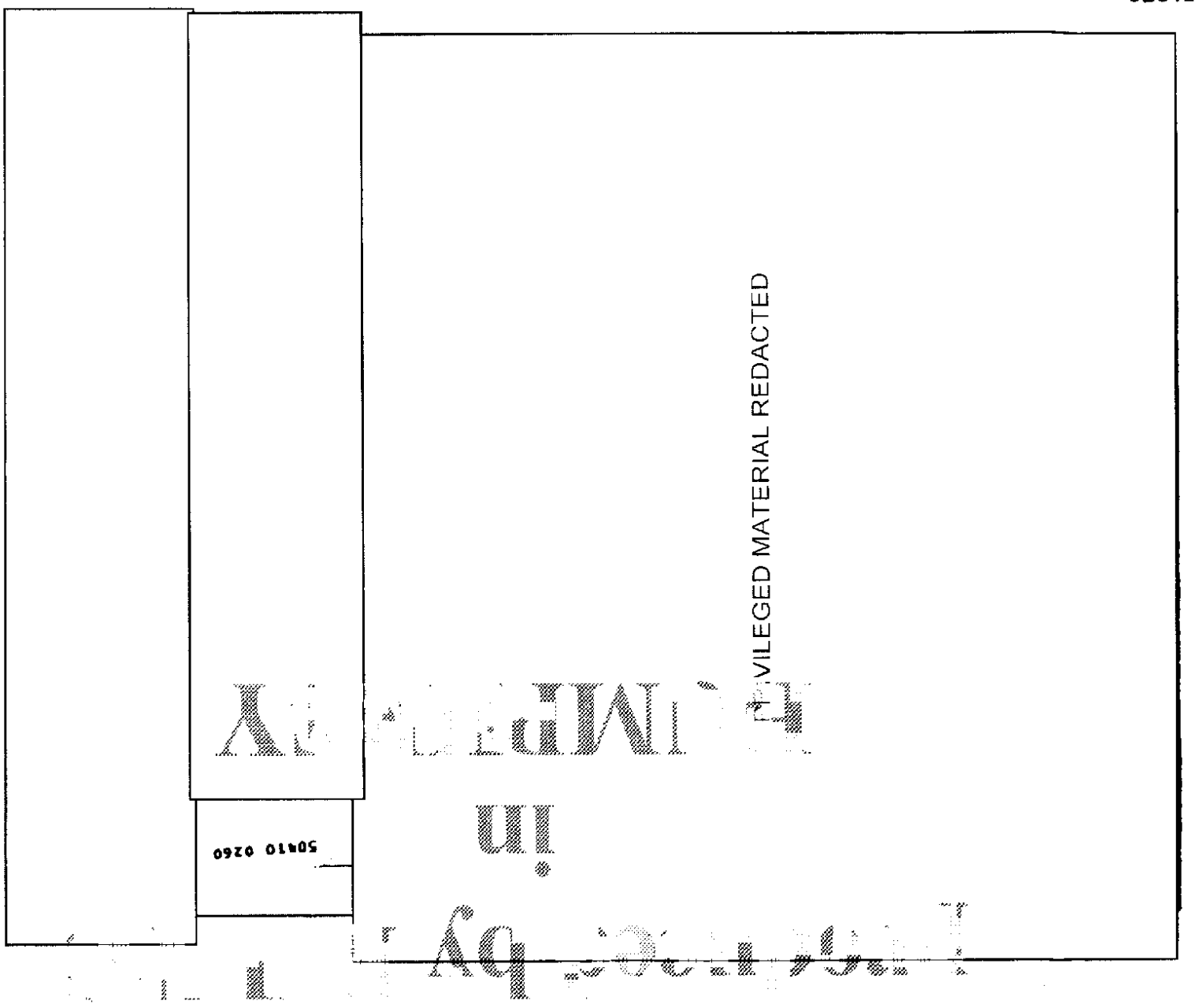

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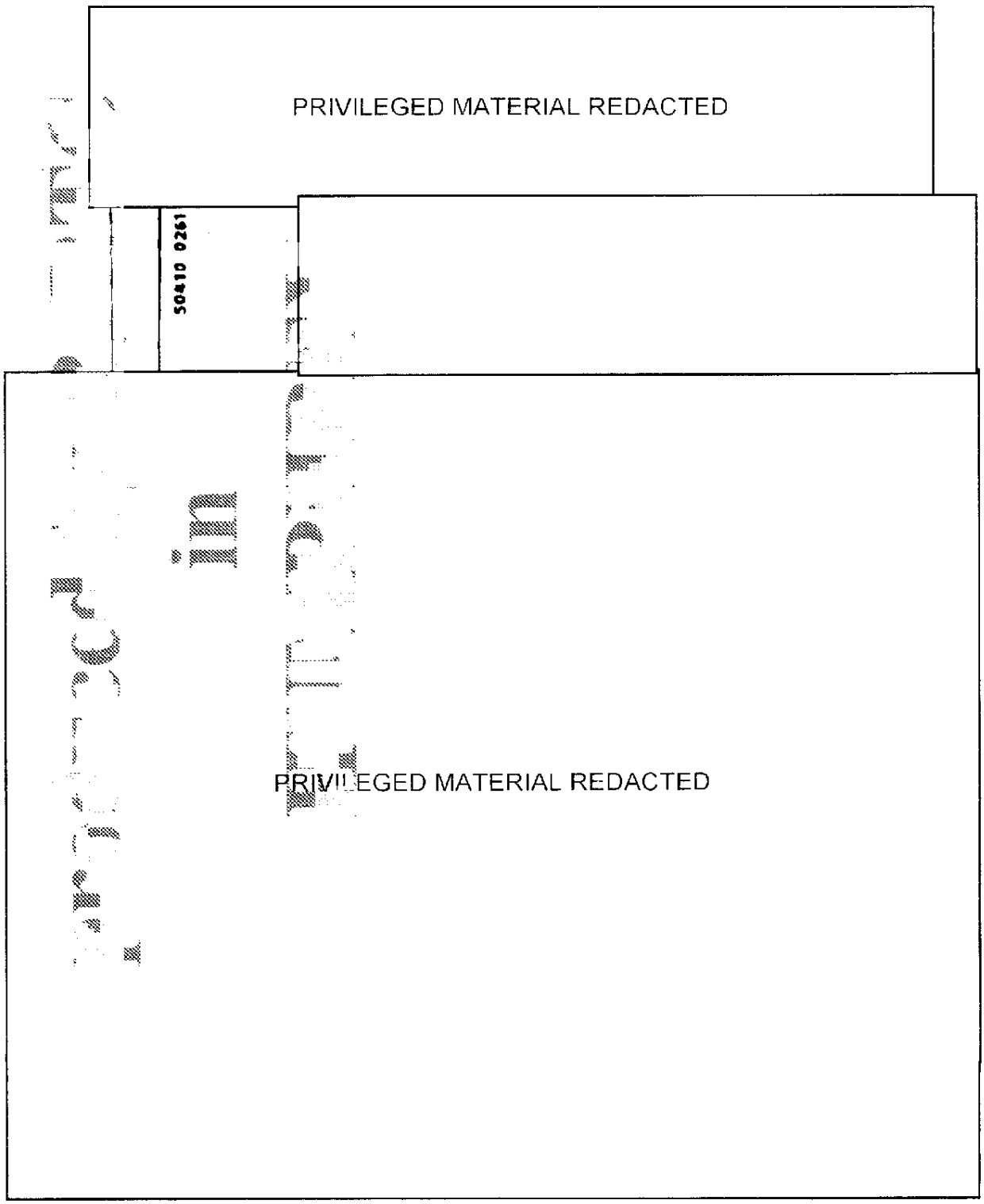

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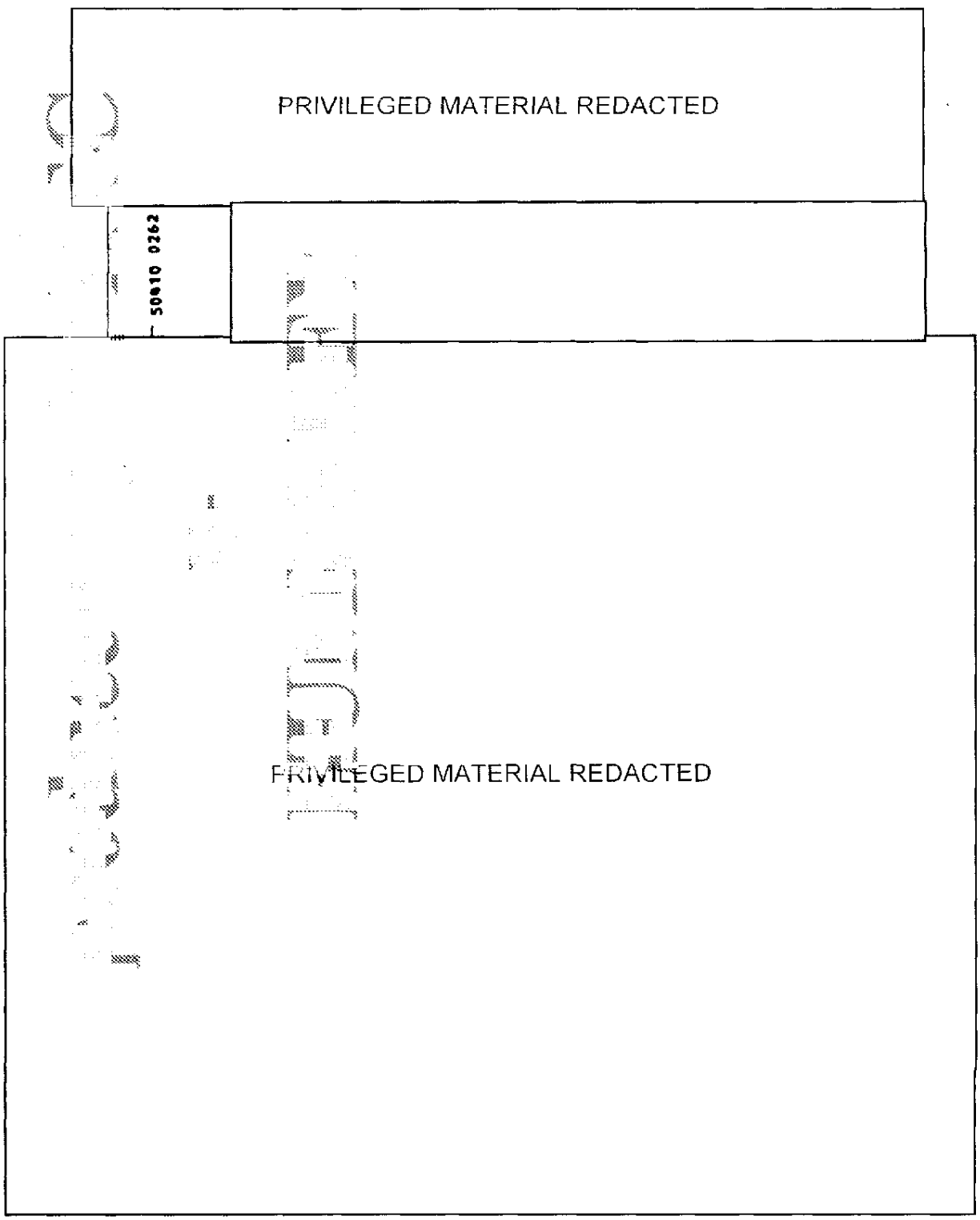

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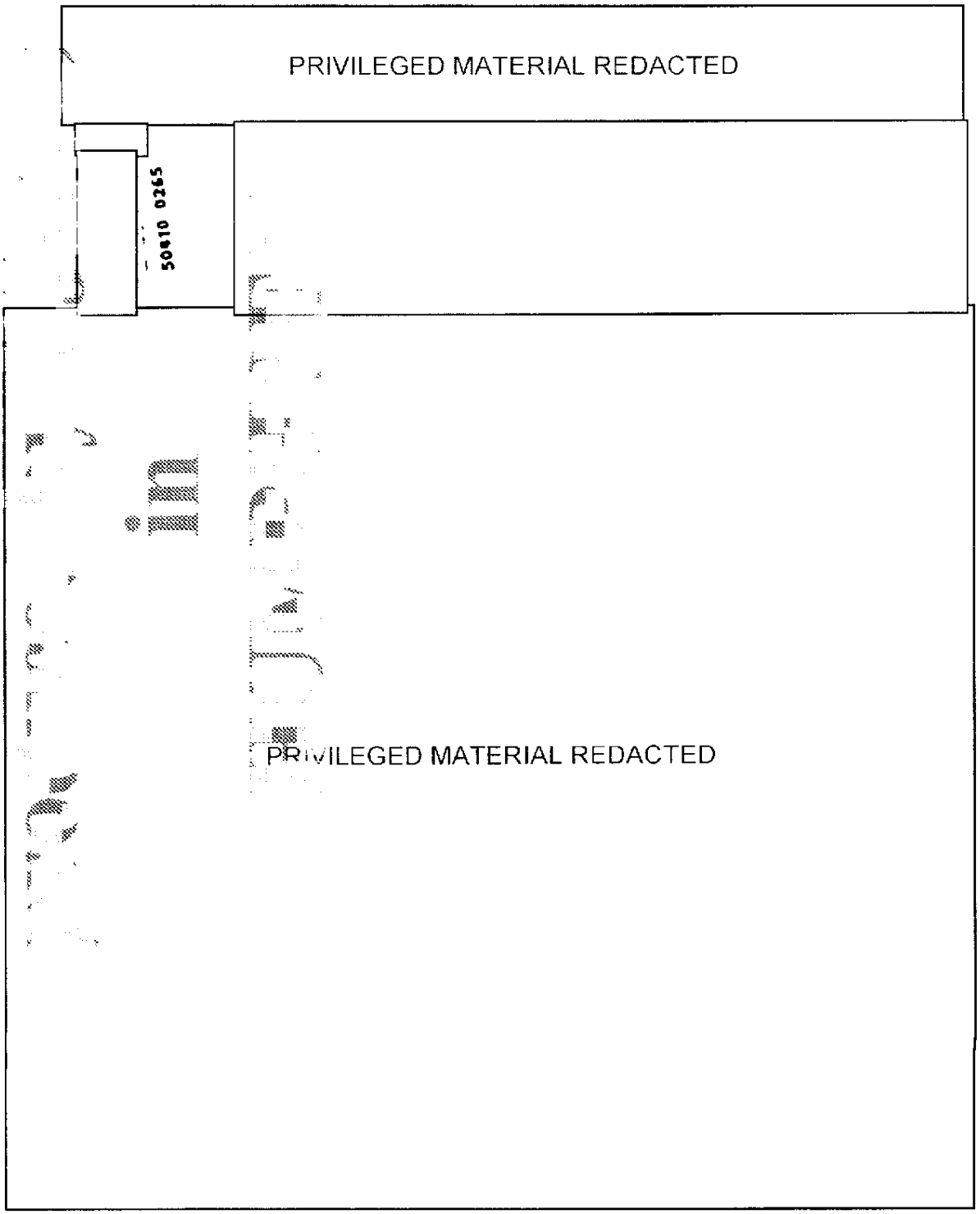

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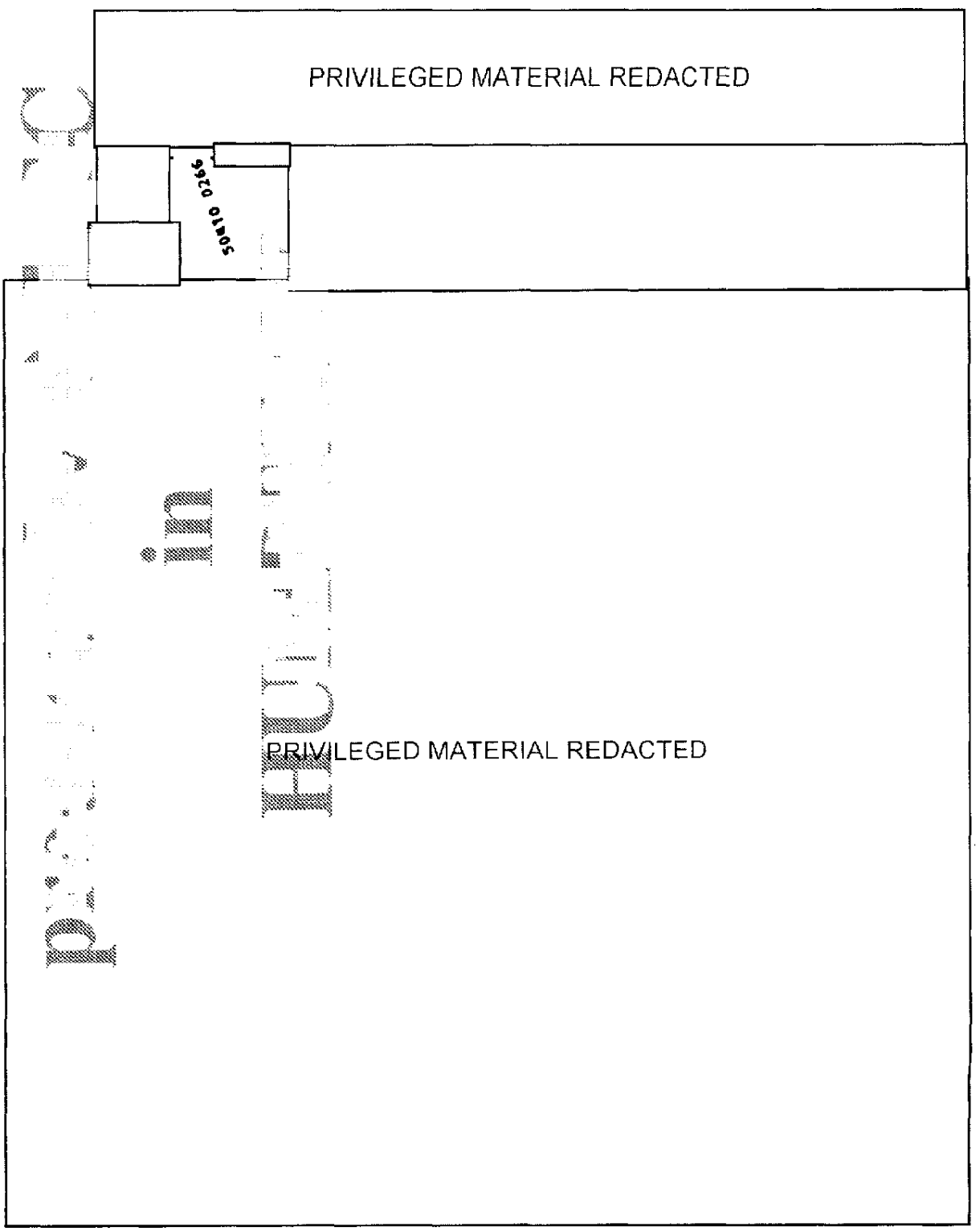

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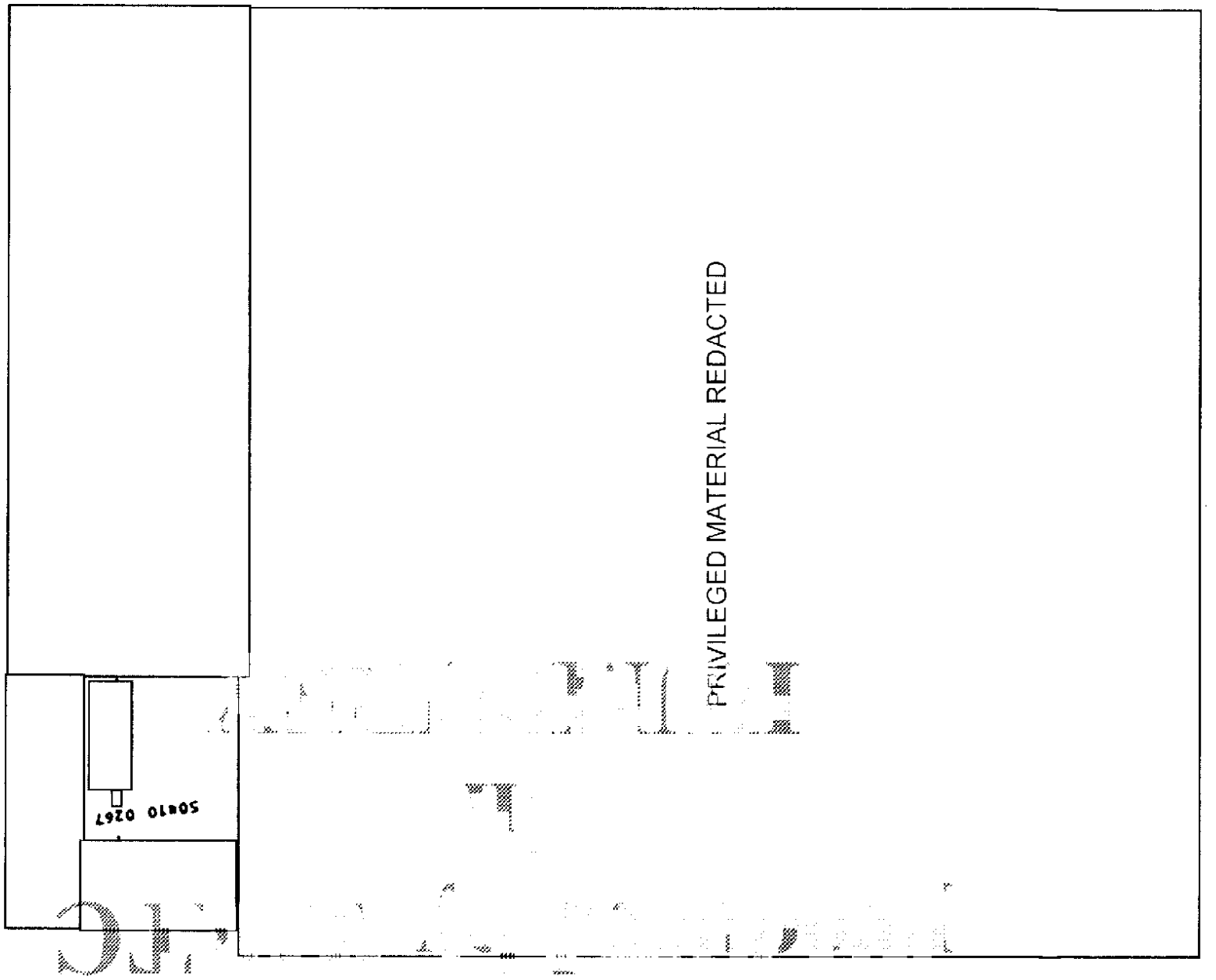

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NOVEMBER 1984 (REVISED)

R. J. REYNOLDS TOBACCO COMPANY
MISSION STATEMENT ON SMOKING AND HEALTH

Produced by R.J.R. Industries BURDEN

THE COMPANY'S VIEWS ON THE SMOKING AND HEALTH CONTROVERSY ARE SIMPLY STATED, THOUGH THEY COVER A VASTLY COMPLEX AREA OF SCIENCE:

- THE SMOKING AND HEALTH CONTROVERSY CONTINUES UNRESOLVED. DESPITE CLAIMS ABOUT CIGARETTE SMOKING AND HEALTH, IT HAS NOT BEEN SCIENTIFICALLY ESTABLISHED THAT SMOKING EITHER DOES OR DOES NOT CAUSE DISEASE IN HUMANS.

- DESPITE CLAIMS TO THE CONTRARY, NO INGREDIENT OR GROUP OF INGREDIENTS, ASSERTED IN TOBACCO SMOKE, HAS BEEN PROVEN TO BE A CAUSE OF DISEASE IN HUMANS.

- THE SIMPLE AND UNFORTUNATE FACT IS THAT SCIENTISTS DO NOT KNOW THE CAUSE OR CAUSES OF THE DISEASES REPORTED TO BE ASSOCIATED WITH SMOKING. NOR DO THEY UNDERSTAND THE MECHANISM OR MECHANISMS WHEREBY THESE DISEASES DEVELOP. MUCH MORE RESEARCH IS NECESSARY BEFORE SCIENCE CAN DETERMINE THE CAUSES AND MECHANISMS OF THESE DISEASES.

- THERE IS A SIGNIFICANT BODY OF INFORMATION THAT IS CONTRARY TO THE HYPOTHESIS THAT SMOKING CAUSES OR CONTRIBUTES TO DISEASE CAUSATION. HOWEVER, THERE IS A LARGE AND WIDELY-CITED BODY OF INFORMATION AND OPINION (BASED LARGELY ON STATISTICS) IN SUPPORT OF THE CONCLUSION THAT,

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ALTHOUGH THE SPECIFIC MECHANISMS OF DISEASE CAUSATION HAVE NOT BEEN PROVEN, CIGARETTE SMOKING MAY BE A CAUSE OR CONTRIBUTING FACTOR IN DISEASE CAUSATION IN HUMANS.

- IN VIEW OF THE CONTROVERSY SURROUNDING OUR PRODUCTS, THE COMPANY IS COMMITTED TO CONTINUED FUNDING OF ONGOING PROGRAMS OF BIOMEDICAL RESEARCH CONCENTRATING BOTH ON SMOKING AND HEALTH AND ON THE CAUSES AND MECHANISMS OF VARIOUS CHRONIC DEGENERATIVE DISEASES, PARTICULARLY THOSE REPORTED TO BE STATISTICALLY ASSOCIATED WITH SMOKING.*

- THIS RESEARCH WILL CONTRIBUTE TO AN UNDERSTANDING OF WHETHER OR NOT SMOKING PLAYS A ROLE IN THE CAUSATION OF THESE DISEASES; AND IF IT DOES, AN UNDERSTANDING OF WHAT THAT ROLE MIGHT BE.

- THE COMPANY IS COMMITTED TO RESPOND TO THAT BODY OF KNOWLEDGE WHICH CLAIMS OUR PRODUCTS OR THEIR INGREDIENTS, SINGLY OR IN COMBINATION, CAUSE DISEASE. AND WE MUST RESPOND WHETHER OR NOT WE BELIEVE THESE CLAIMS TO BE SCIENTIFICALLY PROVEN. THIS LEADS DIRECTLY TO CERTAIN OF R&D'S OBLIGATIONS AS LISTED BELOW, TO WHICH OUR BIOCHEMICAL/BIOBEHAVIORAL PROGRAM IS DIRECTED.

*THROUGH THE CTR, THE COMPANY'S MRP, AND SECTIONS OF THE RJRI BASIC RESEARCH PROGRAM.

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HUMPHREY

REC'D APR 6 1988

Can we have an open debate about smoking?

The issues that surround smoking are so complex, and so emotional, it's hard to discuss them objectively.

In fact, many of you probably believe there is nothing to debate.

Over the years, you've heard so many negative reports about smoking and health—and so little to challenge these reports—that you may assume the case against smoking is closed.

But that is far from the truth.

Studies which conclude that smoking causes disease have regularly ignored significant evidence to the contrary. These scientific findings come from research completely independent of the tobacco industry.

We at R.J. Reynolds think you will find such evidence very interesting.

Because we think reasonable people who analyze it may come to see this issue not as a closed case, but as an open controversy.

We know some of you may be suspicious of what we'll say, simply because we're a cigarette company.

We know some of you may question our motives.

But we also know that by keeping silent, we've contributed to this climate of doubt and distrust. We may also have created the mistaken impression that we have nothing to say on these issues.

That is why we've decided to speak out now, and why we intend to continue speaking out in the future.

During the coming months we will discuss a number of key questions relating to smoking and health. We will also explore other important issues including relations between smokers and non-smokers, smoking among our youth, and "passive smoking."

Some of the things we say may surprise you. Even the fact that we say them may prove controversial.

But we won't shy away from the controversy because, quite frankly, that's our whole point.

We don't say there are no questions about smoking. Just the opposite. We say there are lots of questions—but, as yet, no simple answers.

Like any controversy, this one has more than one side. We hope the debate will be an open one.

R.J. Reynolds Tobacco Company

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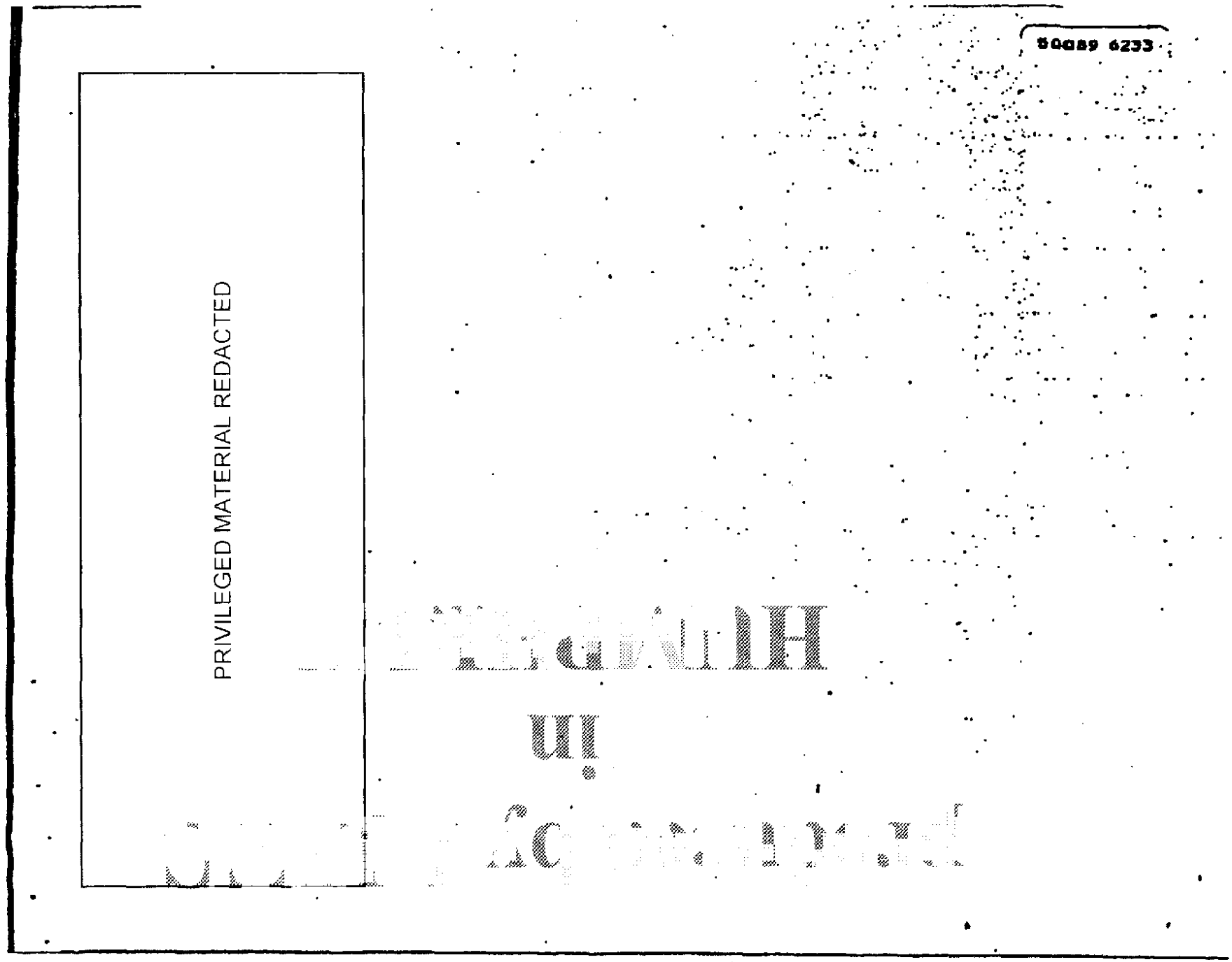

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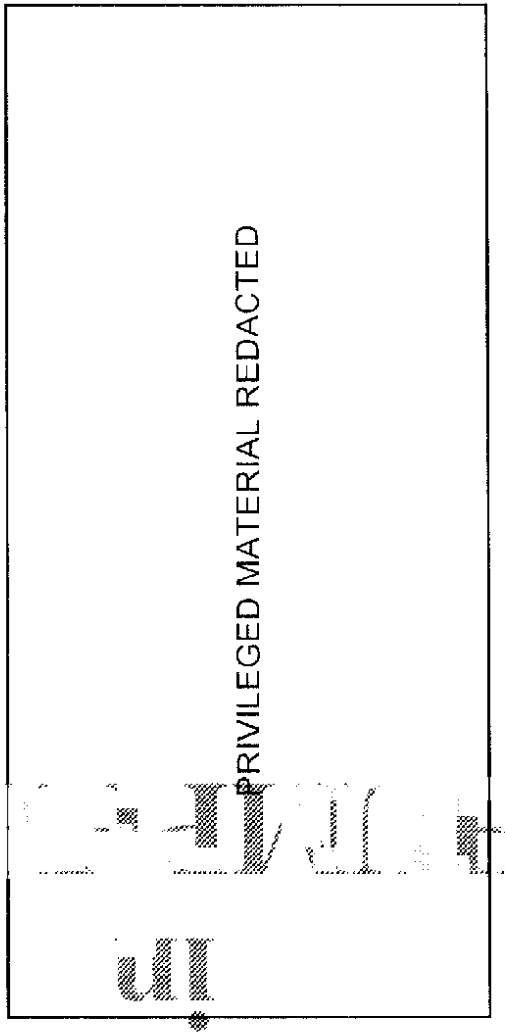

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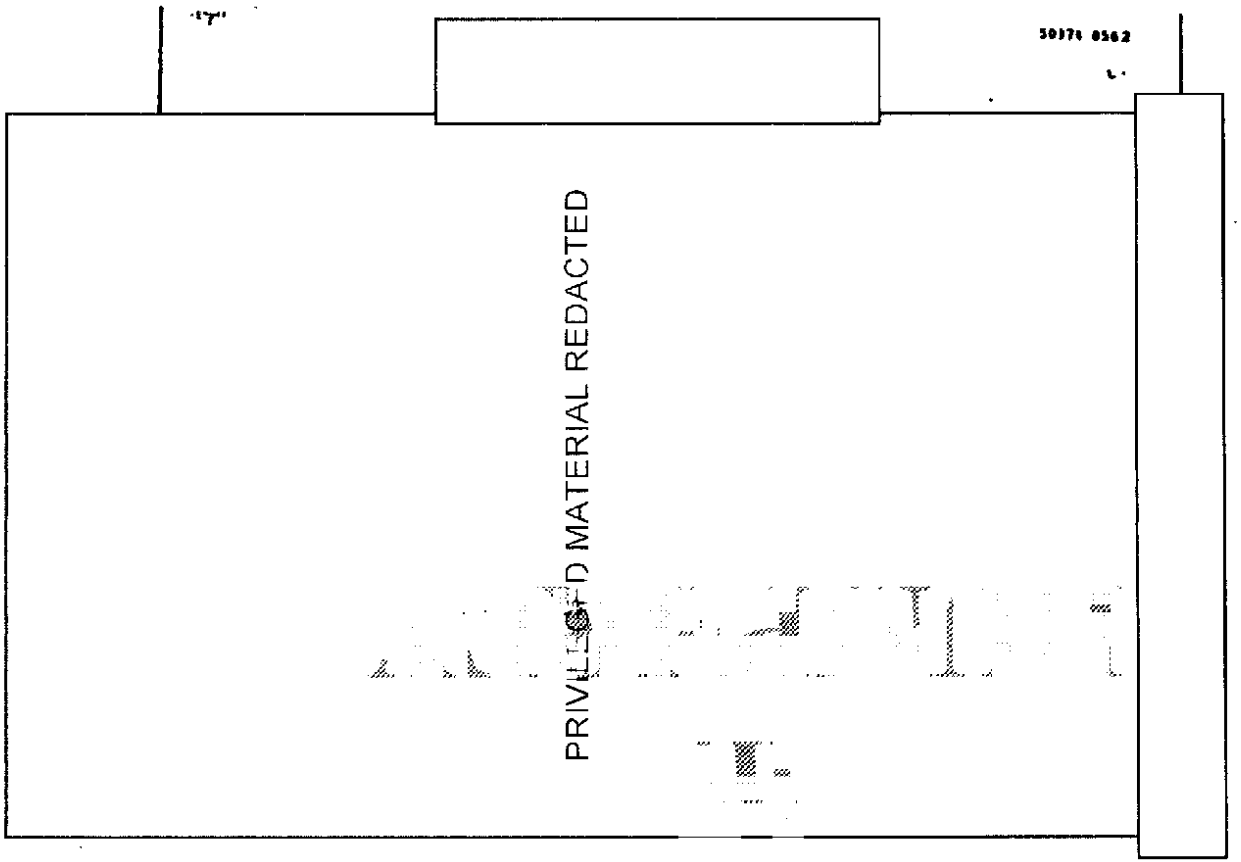

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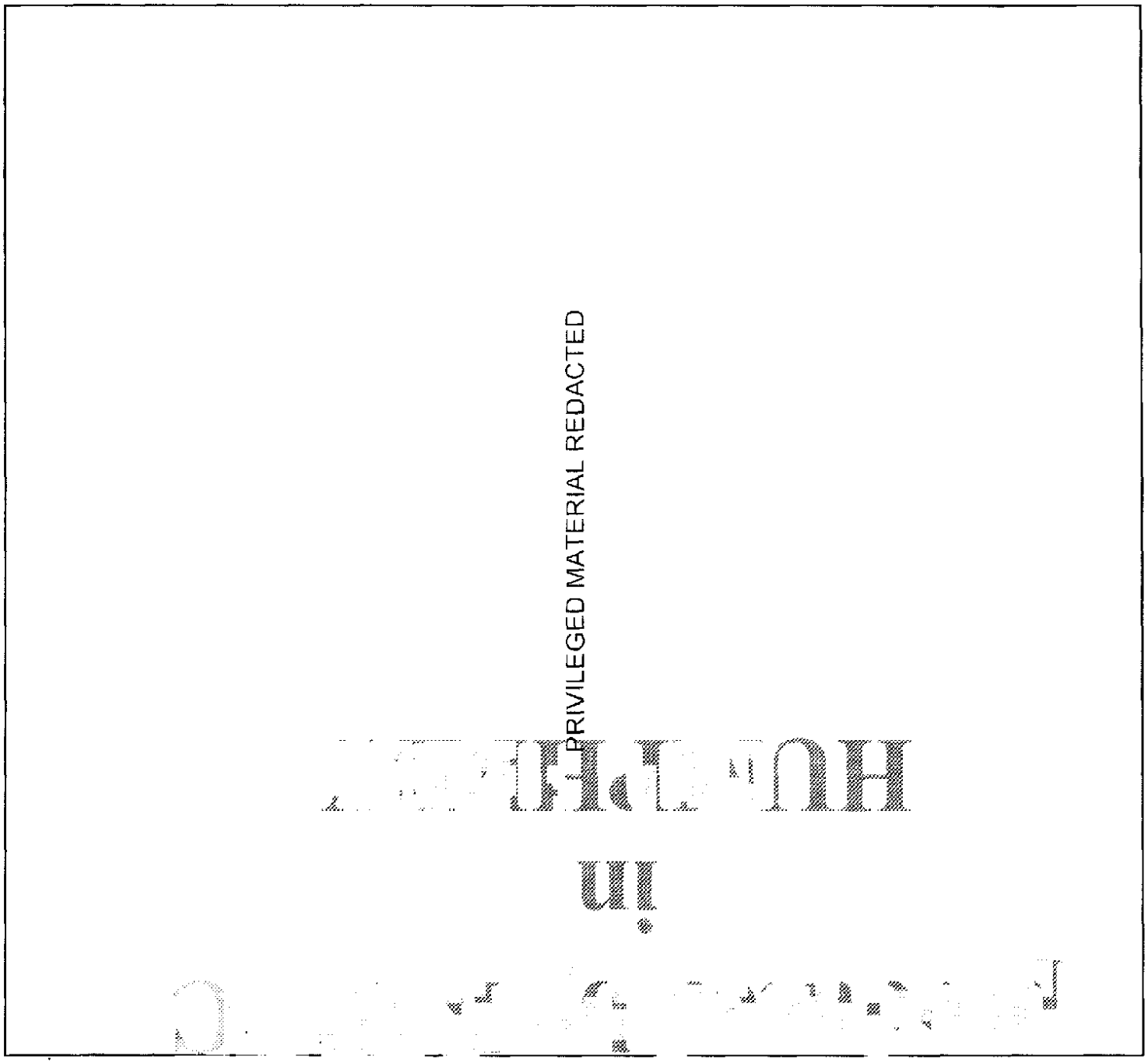

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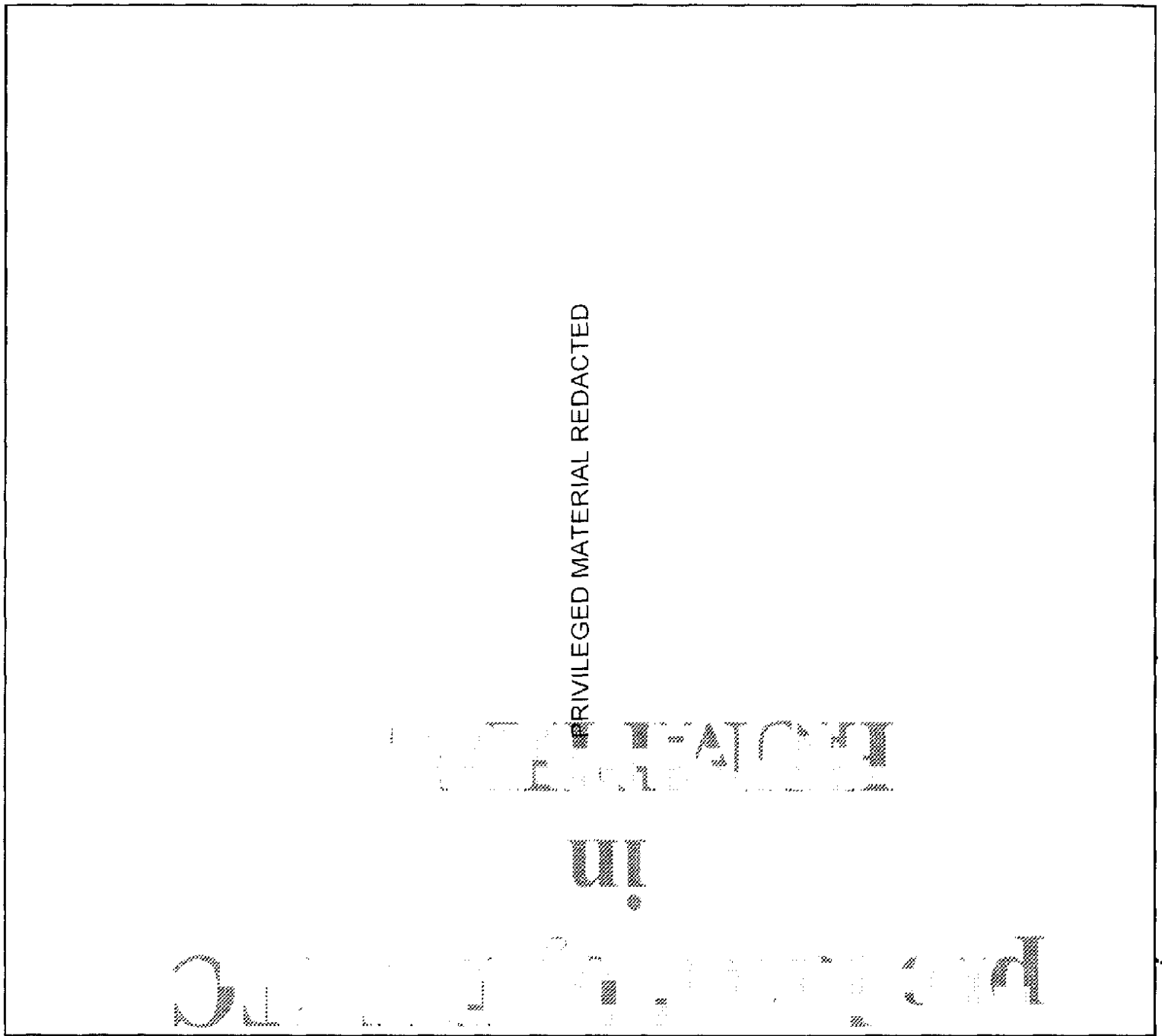

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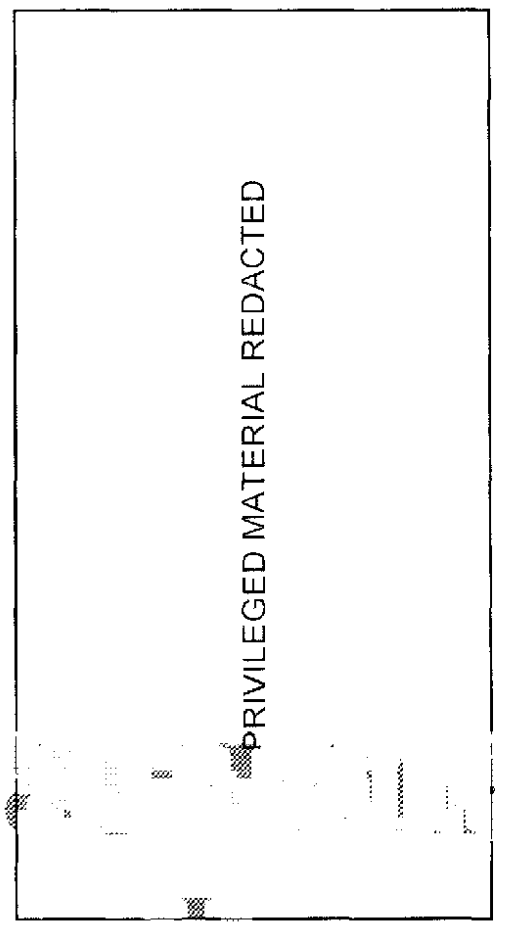

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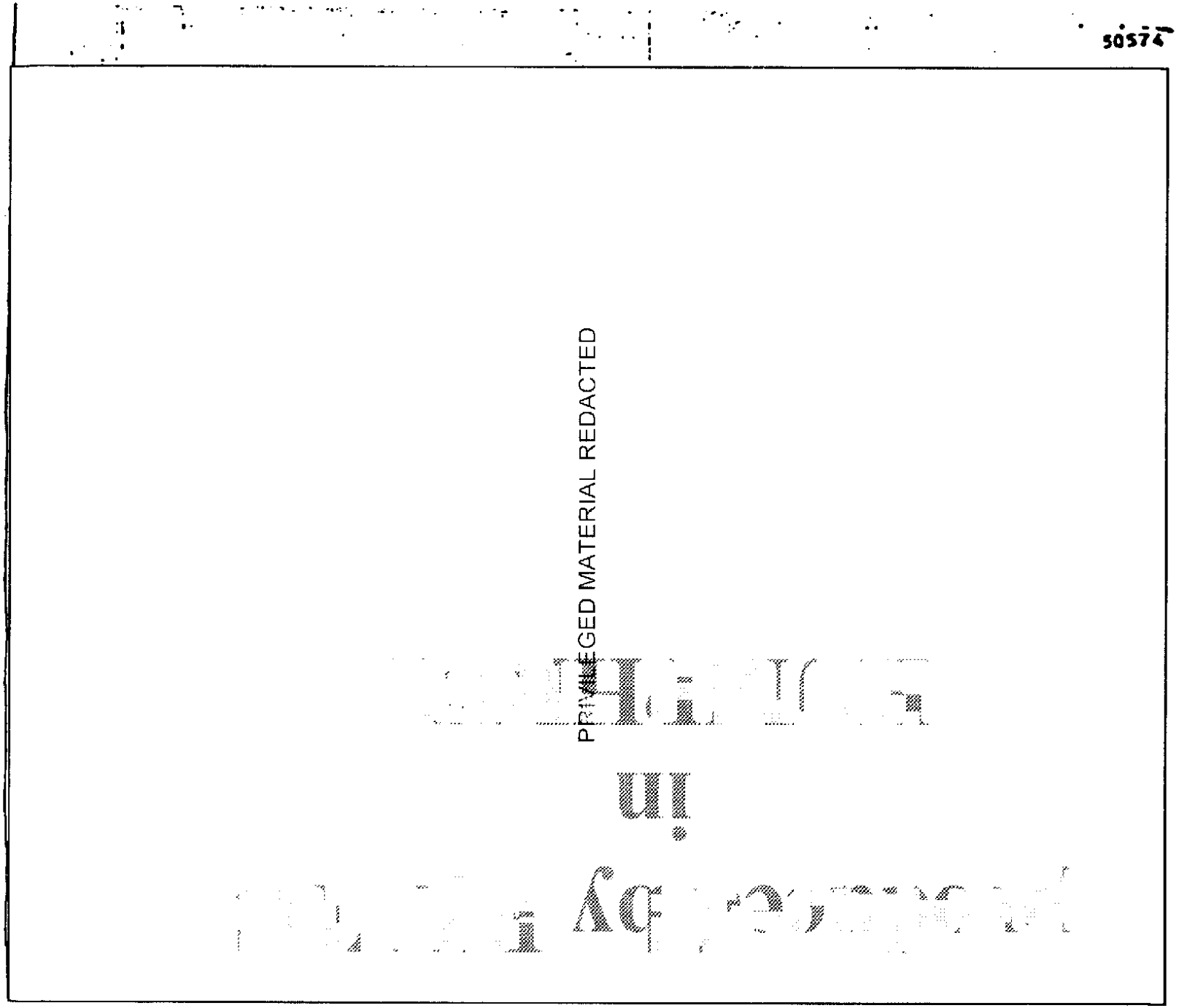

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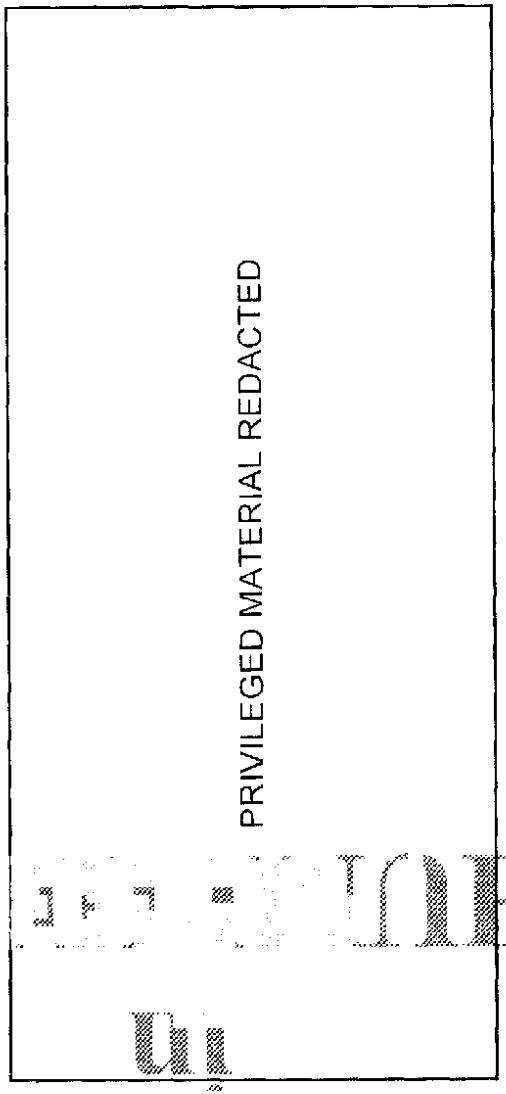

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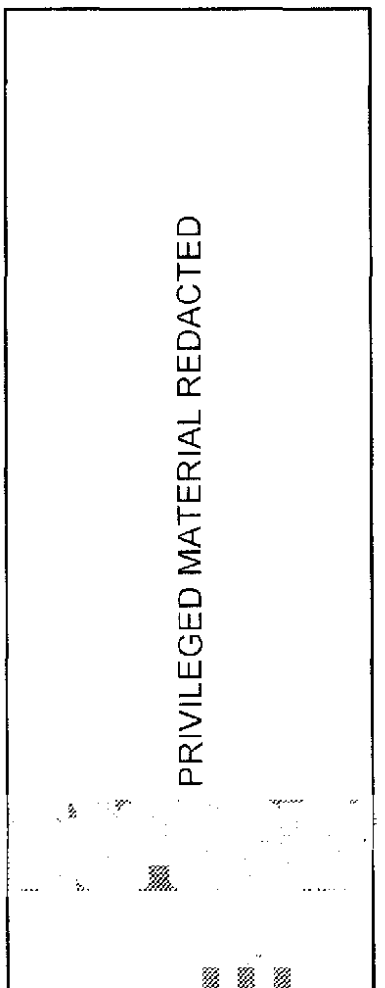

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MEMORANDUM

R.J.Reynolds Tobacco Company
Winston-Salem, N.C. 27102

F.G. Colby
Assistant Director of Scientific Affairs
Research Department

RJR

December 9, 1981

Mr. Jay Giles

RE: Weekly Highlights

- Information was obtained that Philip Morris-U.S.A. does not live up to the alleged 'gentlemen's agreement of not having animal laboratory facilities on their premises in this country. PM indeed has had such facilities for at least 3 - 4 years and continues to operate them. This information was communicated to all concerned.

- A detailed critical assessment was prepared on a paper by Dr. Blackman on smoking and health. The Blackman paper is essentially an endorsement of the 'safer cigarette' concept.

- A number of research proposals to be granted - or not granted - by the Council for Tobacco Research, were assessed at the request of the Legal Department.

- I attended an on-site visit at Battelle/Columbus on their Industry sponsored public smoking project.

FGC/ks

cc: C.W.N.
A.R.

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RJR

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IMPLICATIONS AND ACTIVITIES ARISING FROM CORRELATION OF SMOKE pH WITH NICOTINE INTACT, OTHER SMOKE QUALITIES, AND CIGARETTE SALES

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TABLE OF CONTENTS

		Page
I.	INTRODUCTION; OBJECTIVES	1
II.	HISTORICAL DATA, TRENDS AND BRAND COMPARISONS	1
III.	SMOKE pH AND "FREE" NICOTINE	2
IV.	SMOKE pH AND OTHER SMOKE QUALITIES	2
V.	MARKETING CORRELATIONS AND IMPLICATIONS	3
VI.	PRESENT RJR BRAND ACTIVITY	3
VII.	RESEARCH ACTIVITIES, CURRENT AND PLANNED	4

LIST OF CHARTS

Chart No.	Title	Page
I	pH Concept and Scale	6
II	Puff-By-Puff pH Values: 1972 WINSTON and Marlboro 85	7
III	Average Maximum Smoke pH of Tobacco Materials and Products	8
IV	WINSTON vs Marlboro: Smoke pH vs Year of Manufacture	9
V	SALEM vs Kool: Smoke pH vs Year of Manufacture	10
VI	Filter Cigarette: Smoke pH vs Year of Manufacture	11
VII	Nonfilter Cigarettes: Smoke pH vs Year of Manufacture	12
VIII	pH, Nicotine and Smoke Quality	13
IX	FTC "Tar" and Smoke Nicotine - Marlboro vs WINSTON	14
X	FTC "Tar" and Smoke Nicotine - SALEM vs Kool	15
XI	Sales pH and Free Nicotine - Marlboro vs SALEM	16
XII	Sales pH and Free Nicotine - Kool vs SALEM	17
XIII	Market Share Change vs Free Nicotine in Smoke	18

APPENDICES

Appendix No.	Title	Page
I	Current Data on RJR and Competitive Brands	19
II	Memoranda From Marketing Research	22
III	Present Brand Activity	27

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IMPLICATIONS AND ACTIVITIES ARISING FROM CORRELATION OF SMOKE pH WITH NICOTINE IMPACT, OTHER SMOKE QUALITIES, AND CIGARETTE SALES

I. INTRODUCTION; OBJECTIVES:

This year the continuing, vigorous sales growth of various competitive cigarette brands, especially Marlboro and Kool, prompted an intensive study of the physical and chemical properties of those brands as compared with our brands. This was aimed at (1) identifying any significant property differences which might correlate with market performance, (2) measuring and monitoring such differences, and (3) learning how such differences are achieved, permitting us to achieve similar effects in our existing or new brands, if desired.

II. HISTORICAL DATA, TRENDS AND BRAND COMPARISONS

In seeking out significant property differences, we gathered available historical and current data on our brands and competitive brands, and made comparisons. It soon became apparent that in recent years, corresponding to recent sales performance, the most significant difference between our brands and Philip Morris brands and Kool has been in the area of smoke pH.

It will be recalled that smoke pH is a means for expressing, on a 0-14 scale, the degree of acidity or alkalinity of the smoke system. As smoke pH increases the system becomes more alkaline, and as smoke pH decreases the system becomes more acidic. Chart I* illustrates the pH concept, Chart II shows typical smoke pH curves from which average values are derived, and Chart III shows typical smoke pH data for various tobacco materials and products. Current data on smoke pH and related properties of our brands and competitive brands are given in Appendix I.

Our data show that smoke from our brands, and all other significant competitive brands, in recent years has been consistently and significantly lower in pH (less alkaline) than smoke from Marlboro and to a lesser degree Kool. Chart IV shows averaged smoke pH data for WINSTON vs. Marlboro over the years, Chart V shows a SALEM vs. Kool comparison, and Charts VI and VII show smoke pH data for some other major brands. All evidence indicates that the relatively high smoke pH (high alkalinity) shown by Marlboro (and other Philip Morris brands) and Kool is deliberate and controlled. This has raised questions as to: (1) the effect of higher smoke pH on nicotine impact and smoke quality, hence market performance, and (2) how the higher smoke pH might be accomplished.

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*Charts I - XIII appear on pages 6 - 18.

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III. SMOKE pH AND "FREE" NICOTIN

In essence, a cigarette is a system for delivery of nicotine to the smoker in attractive, useful form. At "normal" smoke pH, at or below about 6.0, essentially all of the smoke nicotine is chemically combined with acidic substances, hence is non-volatile and relatively slowly absorbed by the smoker. As the smoke pH increases above about 6.0, an increasing proportion of the total smoke nicotine occurs in "free" form, which is volatile, rapidly absorbed by the smoker, and believed to be instantly perceived as nicotine "kick". Chart VIII shows how proportion of "free" nicotine increases as pH goes higher.

Marlboro and Kool deliver about the same amounts of total smoke nicotine as do our comparable brands (Charts IX and X). However, Marlboro smoke is typically at pH 6.8-7.3, and Kool smoke is typically at 6.4-6.6, as compared with WINSTON smoke at pH 5.8-6.0 and SALEM smoke at pH 6.0-6.2. Thus, Marlboro and Kool smokes contain more "free" nicotine than our comparable brands, hence would be expected to show more instantaneous nicotine "kick" than our brands. Charts XI and XII show these relationships, along with some comparative sales data to be discussed later.

As a result of its higher smoke pH, the current Marlboro, despite a two-thirds reduction in smoke "tar" and nicotine over the years, calculates to have essentially the same amount of "free" nicotine in its smoke as did the early WINSTON. Over the same period, with some reduction in smoke pH and about two-thirds reductions in smoke "tar" and nicotine, the calculated amount of "free" nicotine in WINSTON smoke has decreased by about two-thirds. Thus, currently the calculated amount of "free" nicotine in Marlboro smoke is almost three times the amount in WINSTON smoke. In Kool vs. SALEM comparisons, much the same pattern emerges over time, although the differences are not as pronounced.

IV. SMOKE pH AND OTHER SMOKE QUALITIES

In addition to enhancing nicotine "kick", increasing the pH (increasing alkalinity) of smoke above about 6.0 causes other changes, particularly when the increase in smoke pH is achieved by adding ammonia to the blend. As smoke pH increases, in general stemmy taste, mouth irritation, flue-cured flavor and Turkish flavor are diminished, and burley flavor and character are enhanced. It should be noted, however, that if the smoke pH goes much above 7 at normal total smoke nicotine levels (1.1-1.6 µg/cigt.), the amount of "free" nicotine becomes high, and this may cause harshness to the throat. These changes in smoke qualities with changes in smoke pH are illustrated in Chart VIII.

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V. MARKETING CORRELATIONS AND IMPLICATIONS

Putting all of this together, we see that Marlboro (and other Philip Morris brands) as compared with WINSTON, our other brands and most other brands on the market shows: (1) higher smoke pH (higher alkalinity), hence increased amounts of "free" nicotine in smoke, and higher immediate nicotine "kick", (2) less mouth irritation, less stemmy taste and less Turkish and flue-cured flavor, and (4) increased burley flavor and character. Kool differs from SALEM in much the same way; however, the differences are not as great and the different levels of menthol and other factors tend to blur the picture.

These differences in nicotine impact and other smoke qualities arising from smoke pH increases would be expected to give rise to differences in consumer response, hence market performance. Our preliminary correlations strongly suggest that this is the case and that the vigorous, sustained growth in sales of Marlboro (and other Philip Morris brands) and Kool correlates closely with the increased smoke pH, hence increased "free" nicotine and nicotine impact of those brands. The accompanying reduction in mouth irritation and stemmy taste, and the increased burley character may also be factors.

Chart XI compares regular WINSTON to regular Marlboro in terms of smoke pH, calculated amount of "free" nicotine in smoke, and annual sales, for recent years. Chart XII compares regular SALEM to regular Kool in the same way. Chart XIII suggests that market performance of various brands correlates positively with total amount of "free" smoke nicotine, and that all brands surveyed having over about 35 micrograms of "free" nicotine/cigarette increased in market share in the period studied.

Subsequent detailed analysis by Marketing Research of our pH and "free" nicotine data along with sales data and other factors has confirmed the strongly positive correlation between "free" nicotine in smoke (determined by pH and total nicotine in smoke) and market share performance. Memoranda in Appendix II summarize the work of Marketing Research.

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VI. PRESENT R&R BRAND ACTIVITY

If our data, correlations and conclusions are valid, then what has emerged is a rather new type of cigarette, represented by Marlboro and Kool, with high nicotine "kick", burley flavor, mildness to the mouth, and increased sensation to the throat, all largely the result of higher smoke pH. There is evidence that other brands which are selling well also have some of these attributes, particularly increased "free" nicotine impact. Because brands of the new type continue to show vigorous growth in sales; because a high proportion of beginning smokers are learning to like Marlboro, the leading brand of the new type; and because we have no current brand in this newly identified, major segment of the market; it has become appropriate for us to consider moving our present brands in the direction of the new type of cigarette and/or creating new products to compete directly in that area of the market.

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Currently, Research, Tobacco Development and Marketing are collaborating on a series of tests aimed at exploring the newly-identified area of the market. The three basic types of products being prepared for evaluation are: (1) direct matches of Marlboro (NFO 10/15) and Kool (NFO 12/3), (2) WINSTON KING (NFO 10/15) and CAMEL FILTER (NFO 10/15) maintaining basic integrity but with smoke pH same as Marlboro, and (3) SALEM KING (NFO 12/3) maintaining basic integrity and menthol level but matching Kool in smoke pH. Work is planned, but NFO target dates are not yet established, for evaluation of similar smoke pH changes in DORAL and VANTAGE.

Additionally, a series of WINSTON-type cigarettes with step-wise increases in smoke pH, with the top-step well above the smoke pH of Marlboro, will be made for evaluation in the first quarter of 1974. Panel testing of these cigarettes should provide information on: (1) the minimum smoke pH change detected by the consumer, (2) changes in satisfaction factors and other smoke qualities associated with small pH changes, (3) the preferred pH range for smoke of a given, normal nicotine content, and (4) the break-over point, beyond which increasing the smoke pH gives smoke which is undesirable and too harsh to inhale.

A memorandum describing these activities and schedules in more detail appears as Appendix III.

VII. RESEARCH ACTIVITIES, CURRENT AND PLANNED

As its part in this collaborative effort, Research has: (1) collected, correlated, interpreted and described to Management data on smoke pH of various brands, (2) developed and put into routine use improved methods for measurement of smoke pH, (3) discovered and reproduced the additives and procedures necessary to prepare the G-7 type of material used to increase the smoke pH of Marlboro, and (4) monitored, on a continuous basis, smoke pH and related properties of Marlboro, other Philip Morris brands, Kool, our brands, and some other competitive brands. Additionally, Research has substantial work in progress on (1) determining how smoke pH elevation and control are achieved in Kool, (2) developing a method for measuring pH of pipe smoke, (3) studying how smoke composition and other things change as pH is changed, and (4) evaluating various methods whereby smoke pH may be increased, with emphasis on ammonia treatments of stem materials.

Methods which may be used to increase smoke pH and/or nicotine "kick" include: (1) increasing the amount of (strong) burley in the blend, (2) reduction of casing sugar used on the burley and/or blend, (3) use of alkaline additives, usually ammonia compounds, to the blend, (4) addition of nicotine to the blend, (5) removal of acids from the blend, (6) special filter systems to remove acids from or add alkaline materials to the smoke, and (7) use of high air dilution filter systems. Methods 1-3, in combination, represent the Philip Morris approach, and are under active investigation. The remaining methods appear less attractive or less practical, and are currently receiving less attention.

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Thus in this continuing, collaborative effort, Research is providing measurements, data, interpretations, new information and discoveries, and technical consultation to TPD, Marketing, and others. We anticipate continued intensive effort in this potentially fruitful area throughout 1974.

Claude E. Teague, Jr.

:jbb

Xc: Dr. Murray Senkus

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CHART I

pH CONCEPT AND SCALE

DEFINITION: pH IS A MEANS FOR EXPRESSING, ON A 0-14 SCALE, THE DEGREE OF ACIDITY OR ALKALINITY OF A SYSTEM.

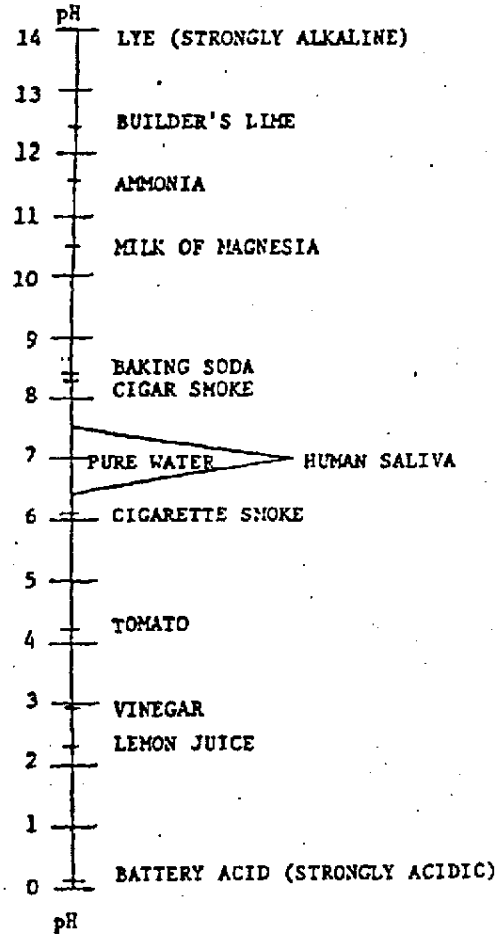

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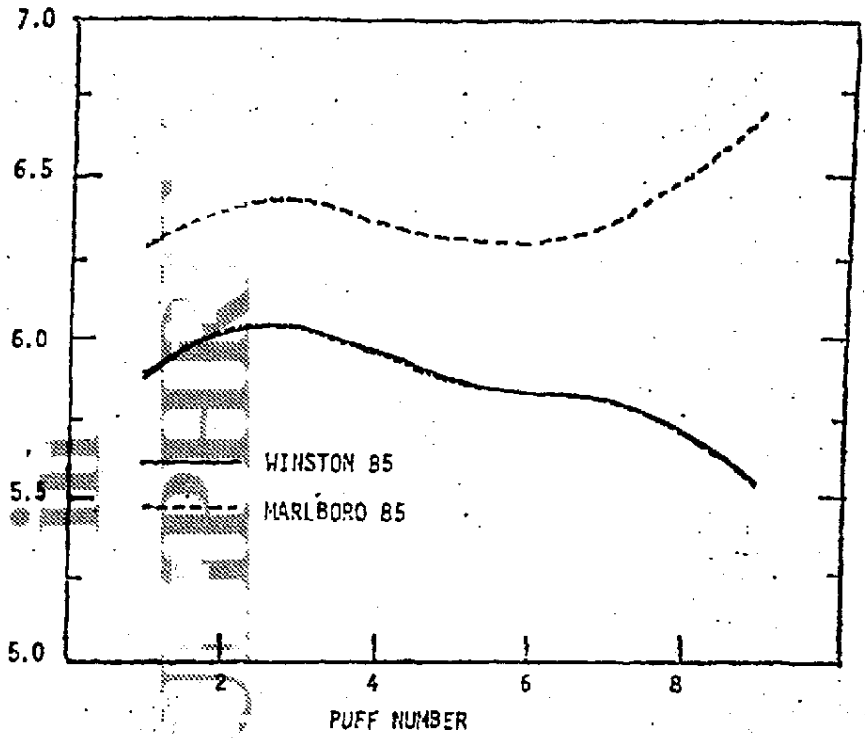
CHART II

PUFF-BY-PUFF pH VALUES:
1972 WINSTON AND MARLBORO B5



Philip Morris Inc.

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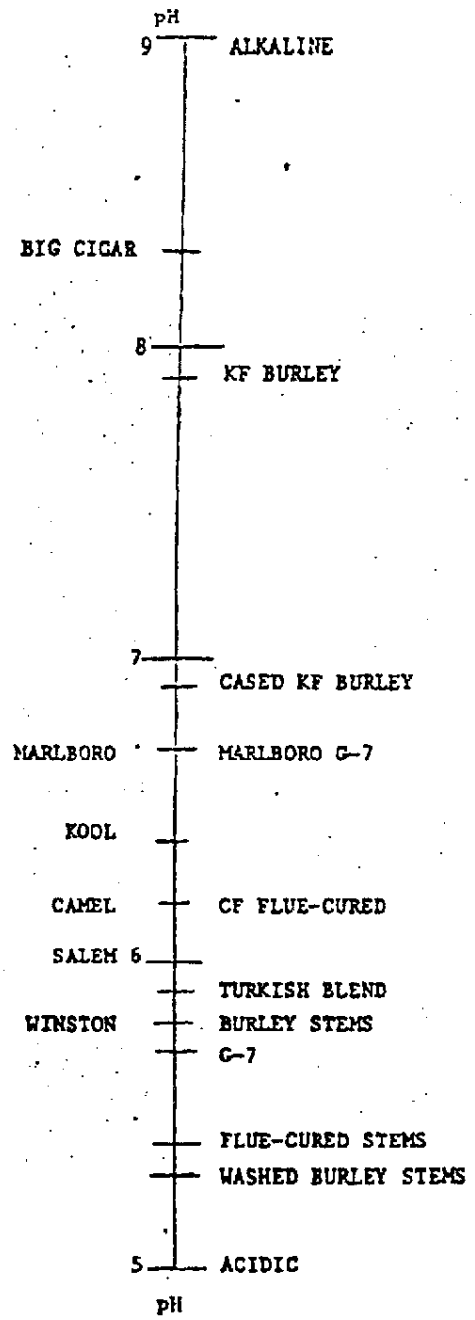
CHART VII

AVERAGE MAXIMUM SMOKE pH OF TOBACCO MATERIALS AND PRODUCTS



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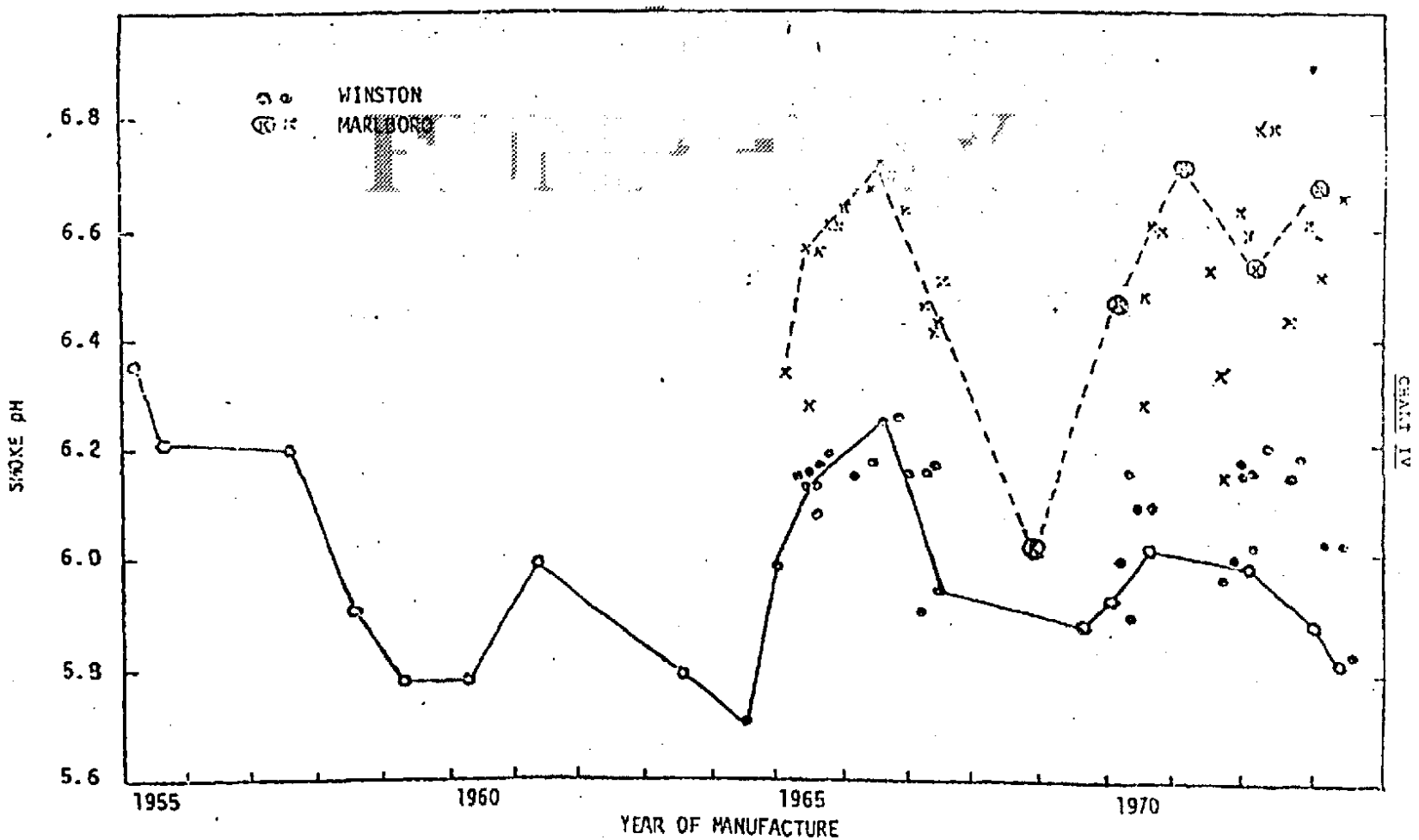

WINSTON VS MARLBORO: SMOKE pH VS YEAR OF MANUFACTURE

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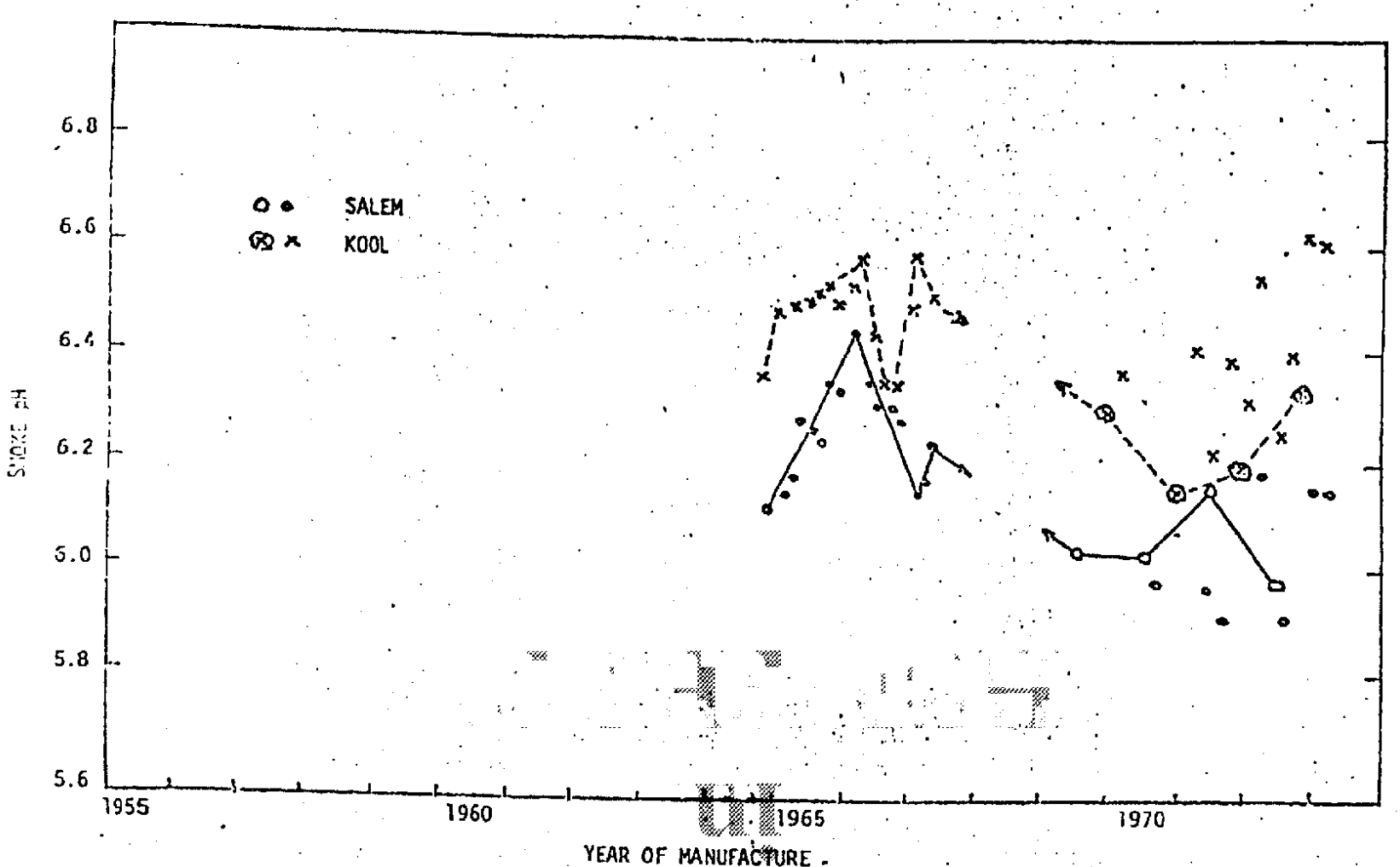

SMOKE PH

CHART V

SALEM VS KOOL: SMOKE PH VS YEAR OF MANUFACTURE

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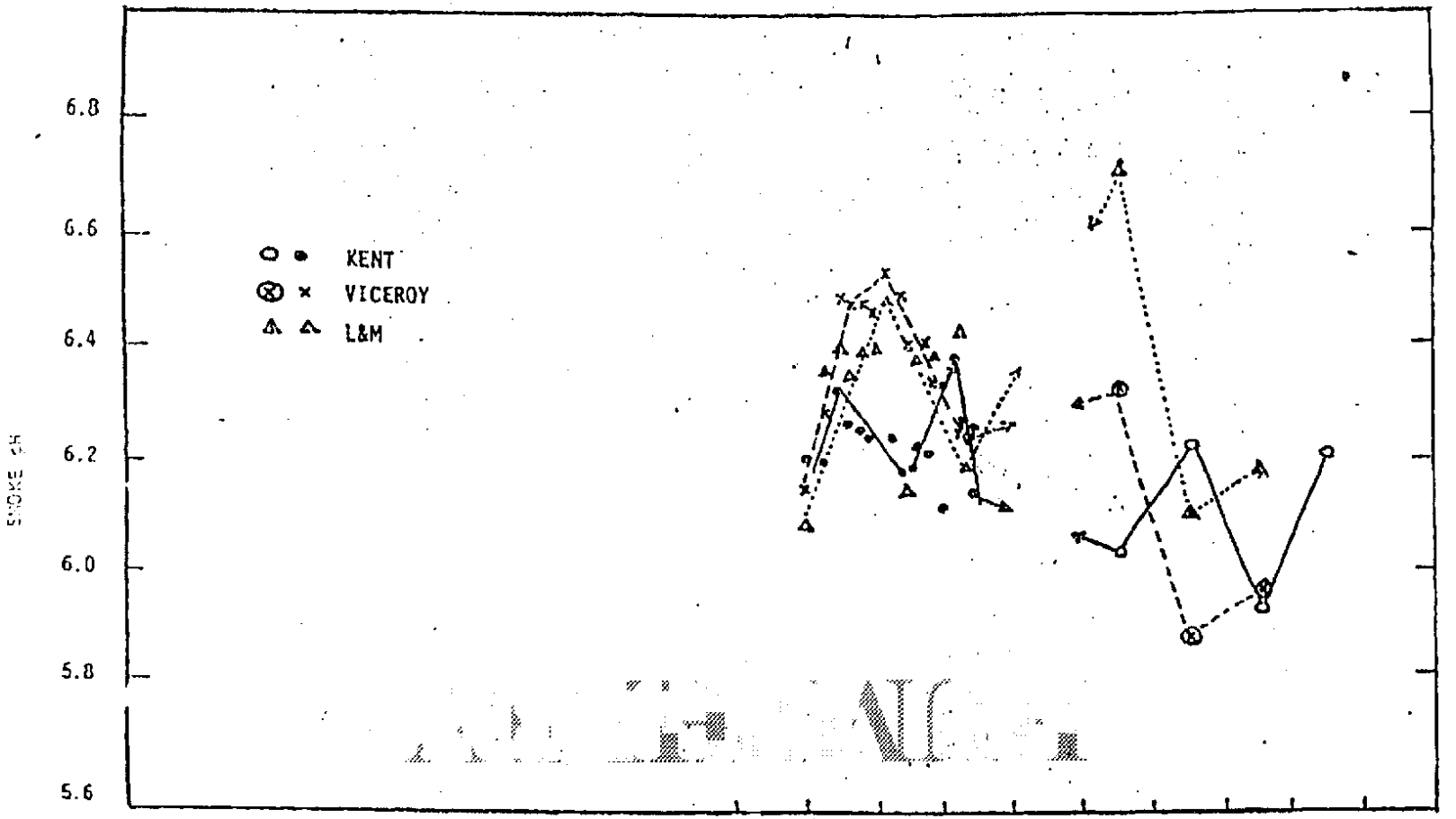

CHART VI

FILTER CIGARETTE: SMOKE pH VS YEAR OF MANUFACTURE

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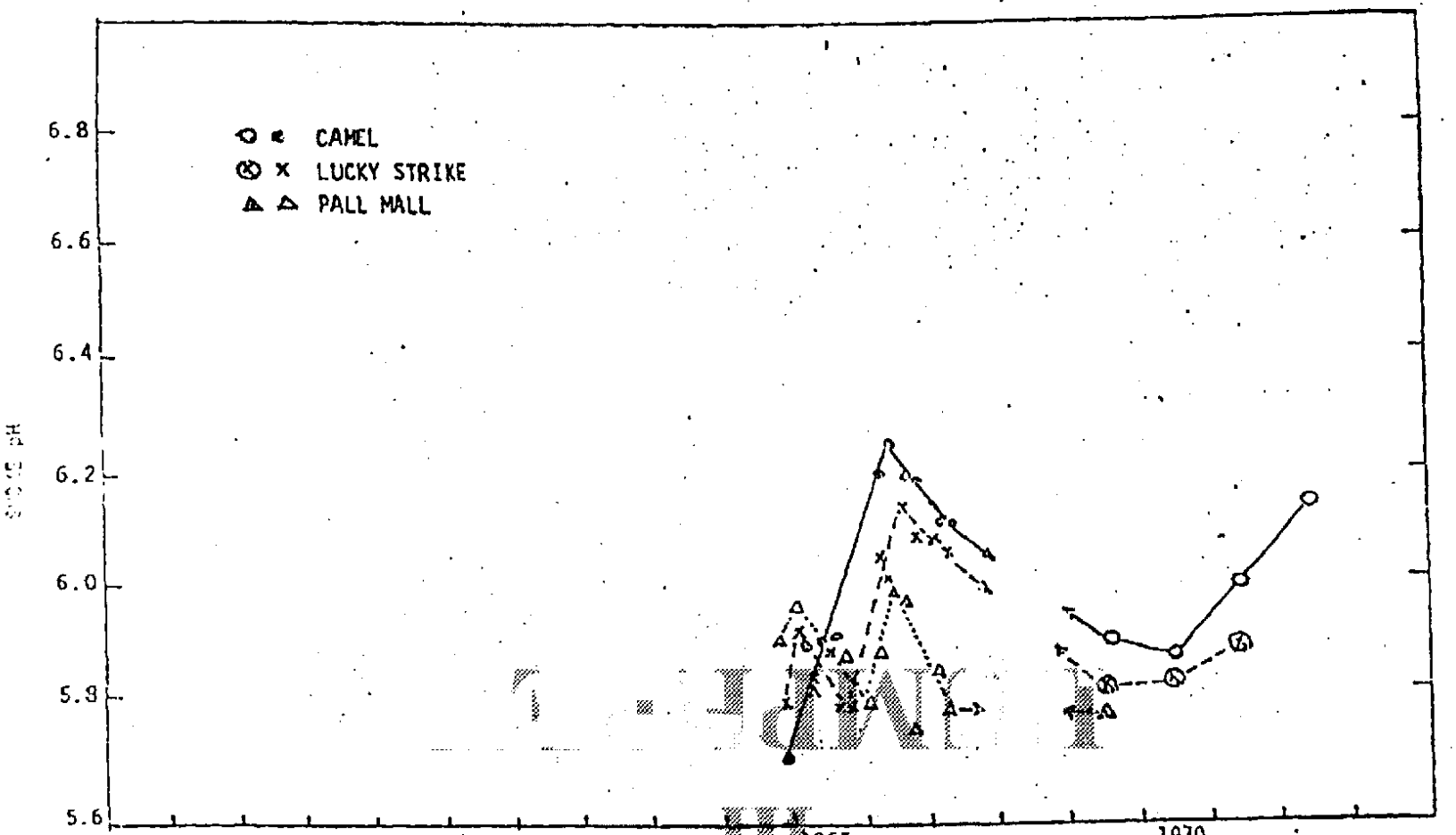

CHART VII

KENTUCKY CIGARETTES: SMOKE PH VS YEAR OF MANUFACTURE

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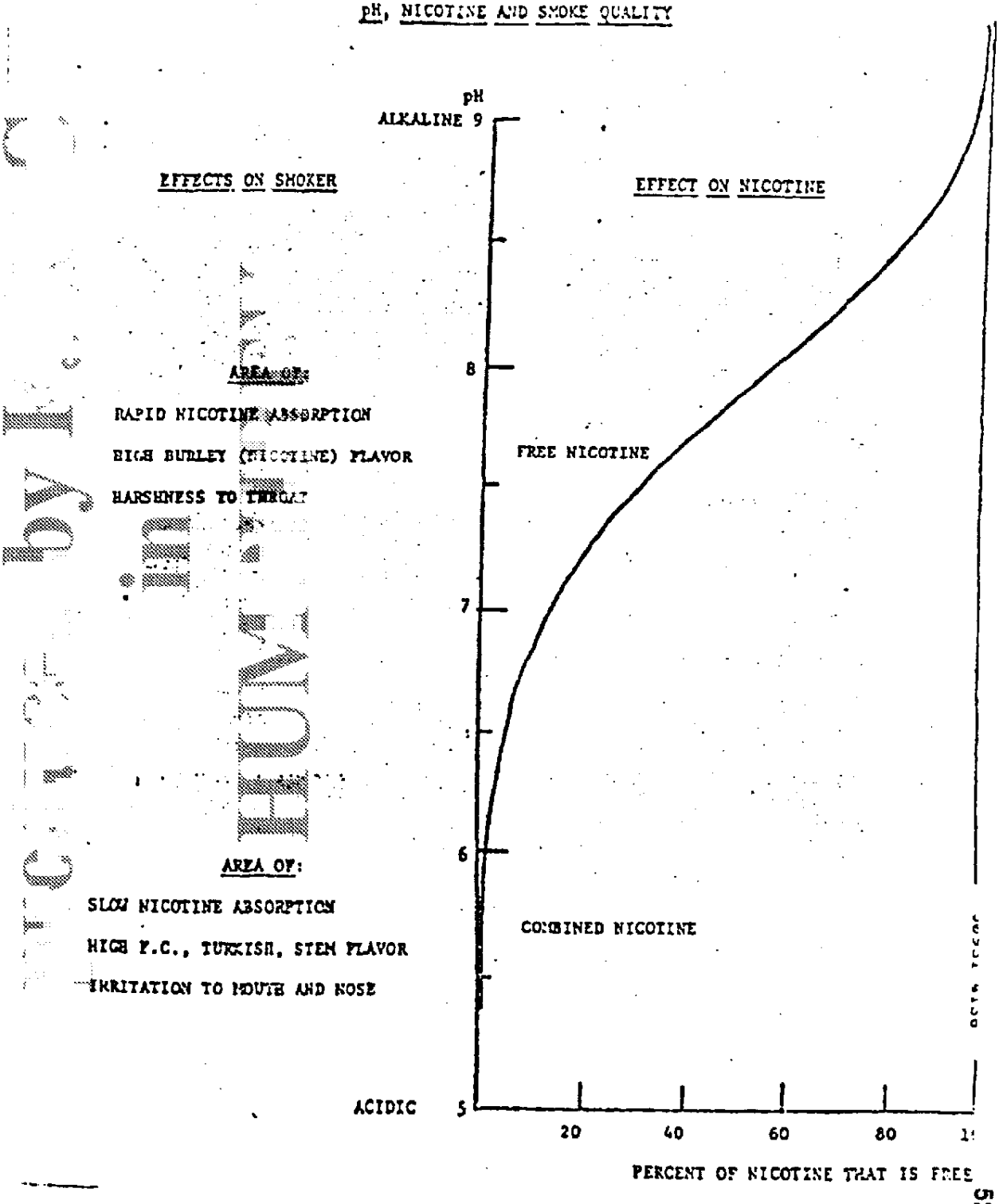
CHART VIII

pH, NICOTINE AND SMOKE QUALITY



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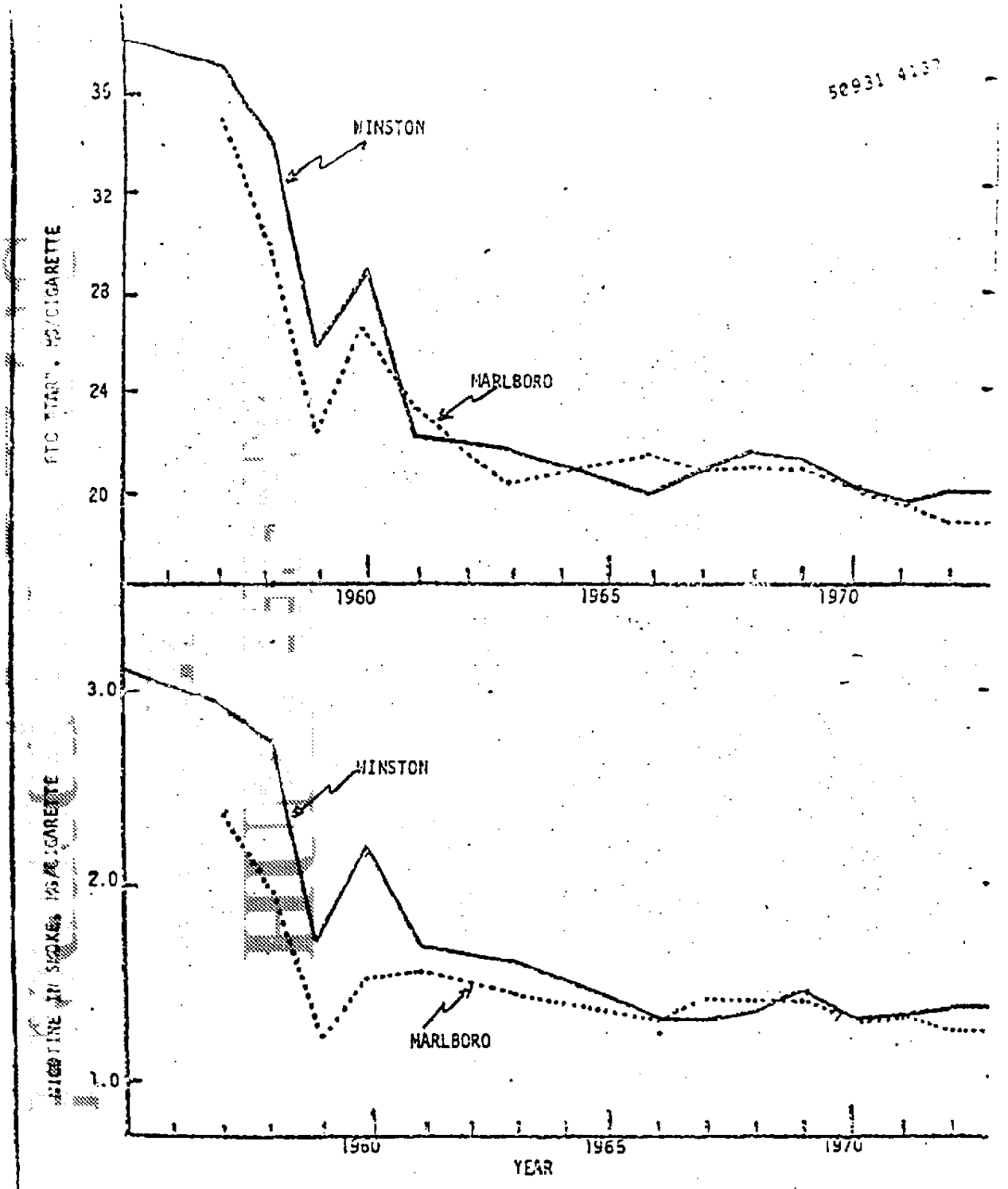

FIG. : FTC "TAR" AND SMOKE NICOTINE - MARLBORO VS WINSTON

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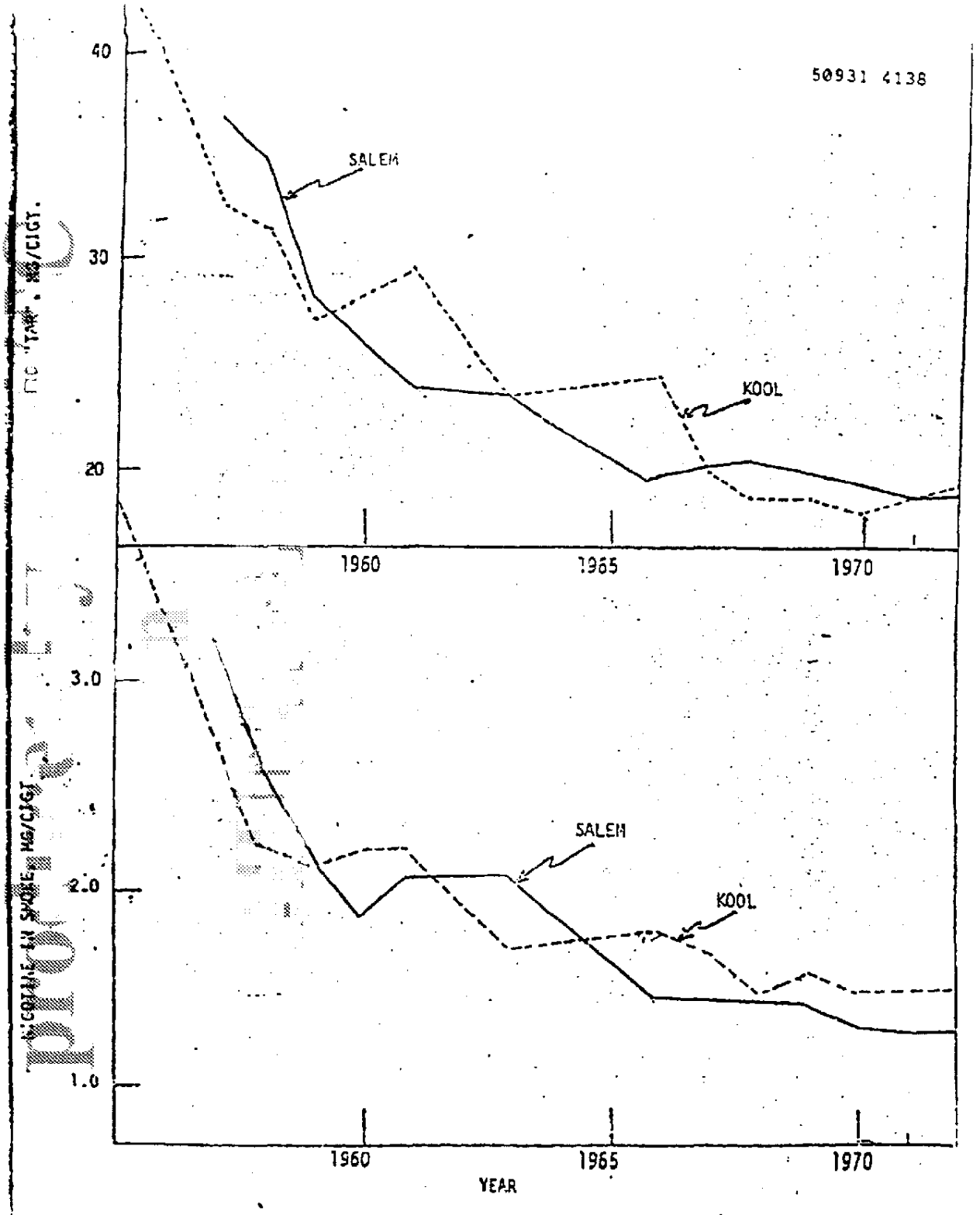

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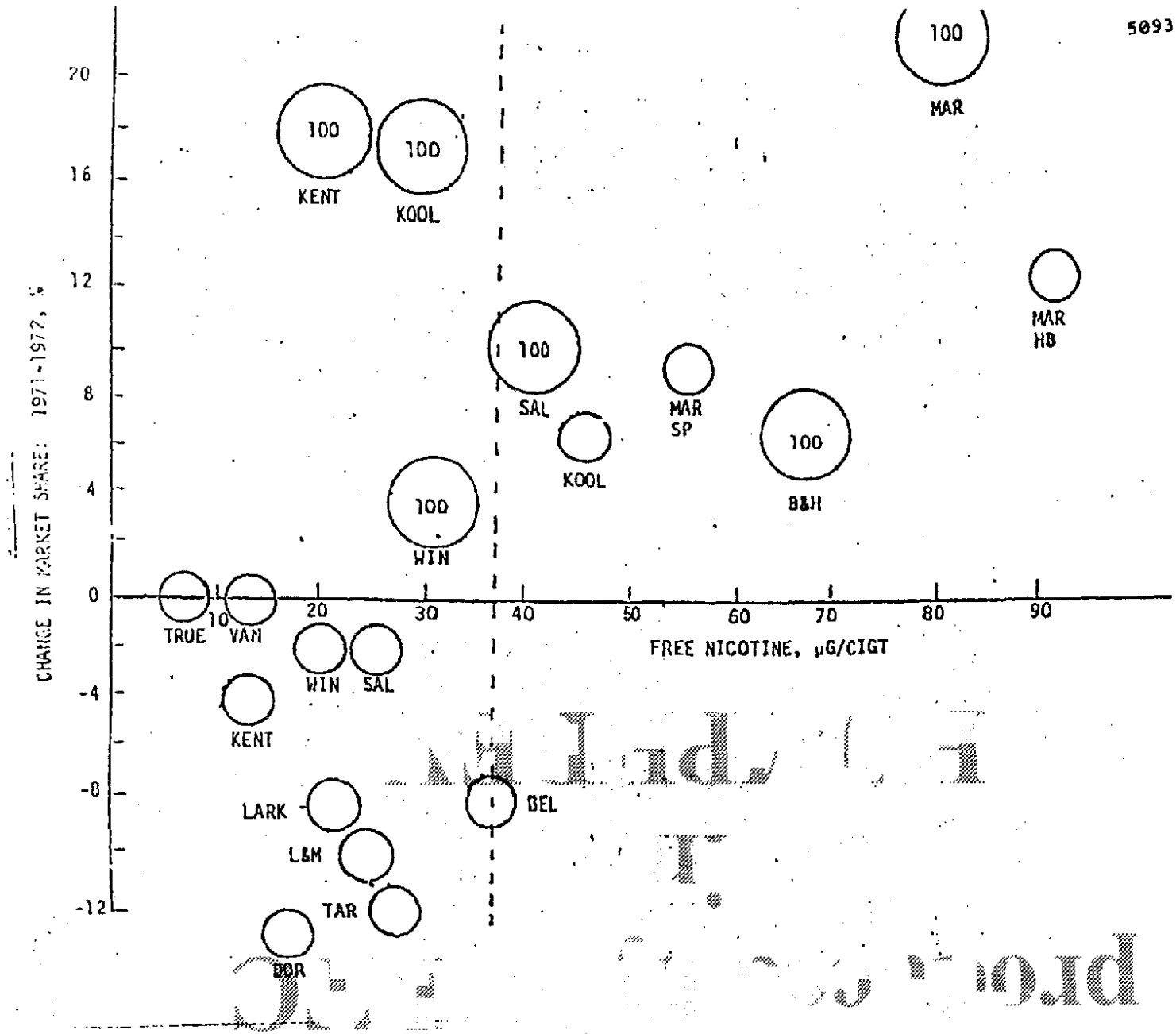

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July 12, 1973

Mr. W. S. Smith, Jr.

Free nicotine does help explain the differences in performance between Winston, Marlboro, Salem and Kool but not all of the difference.

We have reviewed free nicotine, advertising expenditures, and 100mm spin-off data for Winston, Marlboro, Salem and Kool from 1963 through 1972 and found that the difference in share performance of the 85mm styles of each brand is affected by all of the above factors independently and collectively.

Together these three factors statistically explain 97% of the variability between share performance of Winston and Marlboro (King and Box). They explain 95% of the variability between Salem and Kool.

The variability due to "free nicotine" was significant and its contribution was over and above that of advertising expenditures and 100mm spin-off.

Other factors which we reviewed but which did not seem to correlate favorably were:

combined nicotine,
tar,
nitrogen, and
sugar.

Ammonia and out-of-stock conditions look promising, but we have only limited data on both.

Our analysis suggests that pH does not correlate as closely with share performance as does free nicotine. Our emphasis should be directed toward free nicotine while pH would provide us with a measure of or tool to effect free nicotine. We will conduct correlations between performance and pH if you desire.

R. A. Blevins, Jr.

RAB:fm

CC: Mr. W. D. Hobbs
Mr. C. A. Tucker
Mr. C. E. Teague, Jr.

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August 10, 1973

Mr. R. A. Blevins, Jr.

Re: CORRELATION OF pH AND SHARE OF MARKET PERFORMANCE

The correlation of pH and SOM performance holds, but only for those brands having the same nicotine levels. In the analysis of differences in performance between WINSTON and Marlboro and between SALEM and Kool, pH does correlate equally as well with performance as does free nicotine. The total nicotine in WINSTON and Marlboro and in SALEM and Kool is almost equal.

Since pH is a measure of the percent of free nicotine and since the amount of free nicotine present would then depend on the total amount of nicotine, two brands with the same pH could have different amounts of total nicotine and, therefore, different amounts of free nicotine.

Jerry R. Moore
Marketing Research Department

JRM:vhl

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July 3, 1973

Mr. R. A. Blevins, Jr.

Re: CORRELATION OF SMOKE BALANCE FACTORS WITH SOM TRENDS

A preliminary correlation study of smoke balance factors (free nicotine, combined nicotine, tar, nitrogen, ammonia, and sugar) with SOM trends for WINSTON 85's vs. Marlboro 85's and SALEM 85's vs. Kool 85's from 1963 to 1972 confirms the correlation of free nicotine to sales previously reported by Research. Differences in SOM for each year between WINSTON 85's and Marlboro 85's and between SALEM 85's and Kool 85's were correlated with differences in the smoke balance factors (see Table I attached). A correlation of approximately .40 is significant at the 80% level of significance.

While the correlations of differences in SOM with various smoke balance factors (particularly free nicotine) are suggestive, there are other factors, such as differences in advertising expenditures, and differences in SOM of the 100's for the brands also significantly correlated with differences in SOM. Assuming that cause and effect relationships do exist, it is not possible with available data to separate the effects of smoke balance factors and other factors.

In spite of the confounding of effects, a regression model including differences in free nicotine, advertising expenditures, and SOM of the 100's with difference in SOM as the dependent variable resulted in 97% of the variability explained in the case of WINSTON 85's vs. Marlboro 85's and 95% of the variability explained in the case of SALEM 85's vs. Kool 85's. In both cases, free nicotine contributed significantly to the model over and above the other factors.

Jerry R. Moore

Jerry R. Moore

JRM:vl
Attachment

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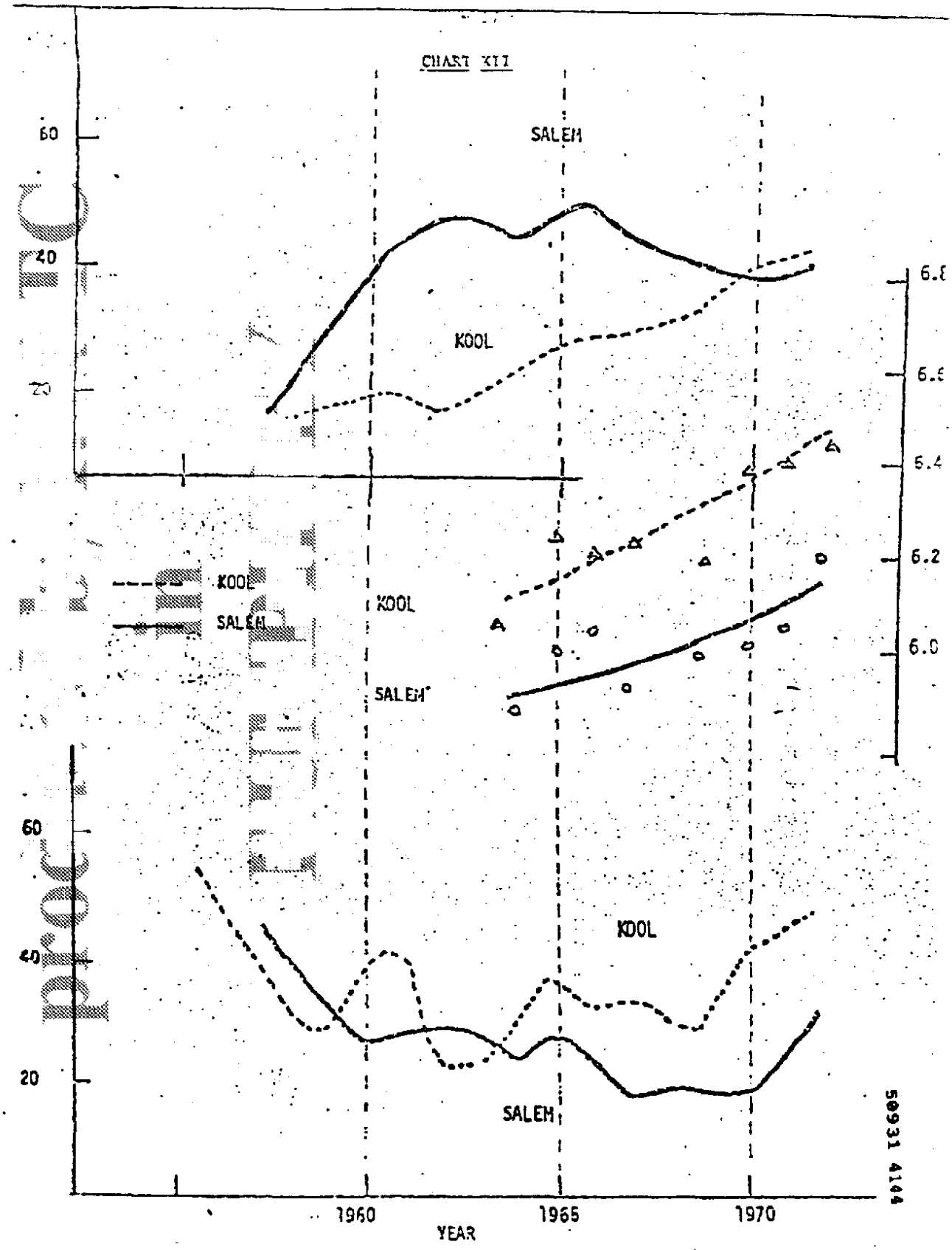

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TECHNOLOGY: AMMONIATION

DEFINITION THE REATION OF AMMONIA WITH TOBACCO TO PRODUCE AMMONIATED TOBACCOS WHICH SMOKE DIFFERENTLY AND PRODUCE A MILDER SMOOTHER FLAVORED SMOKE.

BACKGROUND: RJR BEGAN WORKING WITH AMMONIATION OF TOBACCO AND TOBACCO BY-PRODUCTS IN THE 1950s, BUT DID NOT APPLY THE TECHNOLOGY.

PHILIP MORRIS BEGAN USING AN AMMONIATED SHEET MATERIAL IN 1965 AND INCREASED USE OF THE SHEET PERIODICALLY FROM 1965 TO 1974. THIS TIME PERIOD CORRESPONDS TO THE DRAMATIC SALES INCREASE PHILIP MORRIS MADE FROM 1965 TO 1974.

THE USE OF AMMONIA TO EXPAND TOBACCO WAS INITIATED BY PM IN 1974 AND RESULTED IN AN ADJUSTMENT TO THE PM SHEET MAKING PROCESS.

RJR INTRODUCED AMMONIATED SHEET MATERIAL IN THE CAMEL FILTER PRODUCT IN 1974. BETTER MARKET PERFORMANCE WAS INDICATED IN THE SUBSEQUENT YEARS

LOW "TAR" PRODUCTS AT RJR WERE DESIGNED WITH AMMONIATED SHEET MATERIAL BEGINNING IN 197

RSM STUDIES SHOWED THAT AMMONIATION WAS ONE OF THE MAJOR CONSUMER RECOGNIZED PRODUCT ATTRIBUTES TESTED.

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PLAINTIFFS' EXHIBIT 1062
DATE 6-12-97
WILLIAM D. LABARE
REGISTERED PROF. REPORTER

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AMMONIATED SHEET WAS INTRODUCED INTO THE WINSTON KS PRODUCT IN 1979. MARKET TESTS INDICATED SIGNIFICANT PRODUCT IMPROVEMENT.

RECENT INTERNAL PANEL TESTING OF PRODUCTS WITH AMMONIATED FLUE-CURED TOBACCO HAVE SHOWN CONSISTENT AND SIGNIFICANT PRODUCT IMPROVEMENT.

PRODUCT CHARACTERISTICS:

- MILDER SMOOTHER TASTE
- HIGHER SMOKE pH
- MORE CHOCOLATE-BURLEY TYPE; POSITIVE FLAVOR WITHOUT NEGATIVE BURLEY CHARACTERISTICS
- CLEANER TASTE WITH MORE FREE NICOTINE
- STRONGER PHYSIOLOGICAL IMPACT WITH LESS HARSHNESS
- DIFFERING FLAVOR EFFECTS DEPENDING UPON THE TYPE TOBACCO AMMONIATED.

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TECHNOLOGY: SEGMENTED CIGARETTE

DESCRIPTION: THE ABILITY TO MANUFACTURE CIGARETTES THAT HAVE DIFFERENT MATERIALS IN DIFFERENT PARTS OF THE CIGARETTE. CAN BE THOUGHT OF AS MODULAR CONSTRUCTION OF CIGARETTES. FOR EXAMPLE, THE FIRST HALF OF A CIGARETTE MIGHT CONTAIN ONE KIND OF TOBACCO, THE SECOND HALF OF A DIFFERENT KIND. ON THE FIRST HALF MIGHT BE REGULAR BLEND, THE SECOND HALF MENTHOLATED.

BACKGROUND: NO MANUFACTURING CAPABILITY CURRENTLY EXISTS AT RJR FOR THIS TYPE OF CIGARETTE. WE ARE TRYING TO DETERMINE IF SUCH CAPABILTY EXISTS OR POTENTIALLY EXISTS ANYWHERE.

A HAND OPERATED UNIT TO MAKE SUCH PROTOCEPT CIGARETTES IS BEING USED AT RJR (5 CIGARETTES AT A TIME). COMBINERS USED TO PRODUCE DUAL FILTERS CAN PROBABLY BE USED TO MAKE DOUBLE-WRAPPED SEGMENTED CIGARETTES BY MACHINE.

PRODUCT CHARACTERISTICS: CHANGE (CONTROL) OF STRENGTH AND/OR TASTE AS CIGARETTE IS SMOKED; E.G. STRONGER AT FIRST AND BECOME MILDER OR REGULAR AT FIRST AND CHANGE TO MENTHOL.

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Pltf's Exhibit 1093
Date 7/9/97
DAVID A CAMPEAU

DRAFT 8-9-92

AMMONIA

Ammonia is used by RJRT in the following tobacco processing operations.

(1) Denicotinization of burley tobacco

(2) Ammoniation of reconstituted tobacco

Denicotinization of Burley Tobacco

Denicotinization of some of our burley tobacco gives us greater flexibility in the types of tobacco we can use in our products to meet the constantly changing demands by consumers for cigarette products with different tar and nicotine levels. This process also permits us to partially or completely compensate for the year to year variation in the nicotine content of burley tobacco.

In the RJRT denicotinization process, burley tobacco is first treated with gaseous ammonia and then contacted with steam to remove nicotine and excess ammonia. Since the major portion of the nicotine in the tobacco is present as nicotine salts (citrate, oxalate, malate), the major portion of the residual ammonia is present in the form of the ammonium salts of the acids.

Denicotinization produces the following changes in chemical composition of burley tobacco and smoke: (1) decreased nicotine content of the tobacco; (2) decreased levels of nicotine, related alkaloids, pyrazines and pyridines in the smoke; (3) increased ammonia content of the tobacco; and (4) increased level of ammonia in the smoke.

The magnitude of some of the chemical changes that occur in burley tobacco and smoke are shown in Table I. These data were taken from a report by C. R. Green et al., RDR, 1976, No. 3.

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TABLE 7

EFFECT OF DH PROCESSING ON BURLEY[a] SMOKE AND TOBACCO COMPOSITION

Analysis	LS120A	LS120B	% Difference	LS769A	LS769B	% Difference[b]
Smoke[c]						
TPM, mg	35.0	33.0	ND[d]	37.4	31.9	-15
Water, mg	4.3	3.9	ND	4.3	3.7	-23
Nicotine, mg	4.17	1.80	-57	5.22	1.70	-67
Phenol, mg	26.5	27.2	ND	27.4	26.5	ND
pH	6.9	6.9	ND	6.1	6.9	ND
pH Average Min.	7.01	7.01		7.03	6.66	
pH Average Max.	7.23	6.41		7.89	6.24	
Carbon Monoxide, mg	15.4	17.6	14	19.0	19.4	ND
Formaldehyde, ug	49	50	ND	105	103	ND
Acetaldehyde, ug	955	895	ND	935	930	ND
Acrolein, ug	81	69	-15	93	82	-12
Acetonitrile, ug	87	178	105	123	251	104
Hydrogen cyanide, ug	257	279	ND	314	322	ND
Nitrogen oxides[e], ug	712	752	ND	814	819	ND
Isoprene, ug	835	490	-41	540	470	-13
Phenol, ug	93	81	-15	103	113	ND
Benzo(a)pyrene, ng	11.2	10.7	ND	-	-	-
Weight, g	1.111	1.074				
PD, Inches Water	2.90	2.62				
Sugars, %	1.7	1.4	-17			
Nicotine, %	3.22	1.24	-61			
Ammonia, %	0.70	0.82	17			

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[a]Control Burley = L3120A or L3796A Test Burley = L3120B or L3750B

[b]% difference = 100 (A-B)/B where A = DN burley value, B = Control burley value

[c]Value per cigarette

[d]ND = No difference; values fall within ± 10%

[e]Nitrogen oxides are expressed as NO_2

RJRT is currently using 8-12 percent denicotinized burley tobacco, based on the total blend, in all brands except the NOW Family. The NOW brands contain 15-20 percent denicotinized burley tobacco based on the total blend.

Ammoniation of Reconstituted Tobacco

Studies on the ammoniation of reconstituted tobacco were started in 1973 as a result of R&D studies carried out during the 1950's and early 1970. During the 1950's, Drew, Eldridge, Jr. investigated the ammoniation of tobacco and tobacco constituents and reported dramatic improvements in the smoking qualities of ammoniated tobacco blends. Smoke harshness and irritation were reduced and taste properties were improved.

In the early 1970's, a major R&D program was initiated to investigate the physical chemistry of tobacco and tobacco smoke in an attempt to gain a better understanding of the factors affecting smoke harshness, irritation and strength. These studies led to the following observations and conclusions.

(1) The pH of cigarette smoke is important to smoke quality and can be used as a measure of the physiological strength of smoke.

(2) Ammonia in smoke is one of the major pH controlling components. Others include nicotine, amines, organic acids and carbon dioxide.

(3) Ammonia occurs naturally in tobacco ranging from trace amounts in flue-cured tobacco to over 1 percent in high quality cigar tobacco.

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BIOLOGICAL DATA ON AMMONIA

Ammonia is a normal body constituent which participates in many of the body's catabolic and metabolic processes. Excess amounts of ammonia produced in the body are converted to and excreted as urea in the urine.

Ammonia or its salts are natural components of many of our foods. Also, a number of ammonia-containing compounds are considered GRAS when used as miscellaneous and/or general purpose food additives. These include ammonium hydroxide, ammonium bicarbonate, ammonium carbonate, ammonium saccharin, ammonium sulfate and ammonium phosphate. Other specific applications permit the use of ammonium caseinate, ammonium chloride, ammonium isovalerate, ammonium persulfate, ammonium sulfide, ammonium sulfite, etc. in food products.

It clearly, the use of ammonia in the processes described in this paper are similar to many specific applications commonly used in the food industry. Hence, there would be little reason to expect any undesirable effects.

Although the total ammonia in tobacco smoke can be determined, the actual form of the ammonia is probably as the salts of carbonic acid, isovaleric acid, and other organic acids. Ammonia salts of acids, with the exception of the salts of strong acids such as hydrochloric and sulfuric acid, are usually less irritating and less toxic than free ammonia. Therefore, if we compare the level of total ammonia in cigarette smoke with the known biological effects of ammonia, we are no doubt overestimating any effect.

Acute Toxicity

The acute oral-toxicity (LD_{50}) of ammonia in rats is 350 mg/kg body weight. The maximum exposure for a two-pack-a-day CAMEL Filter smoker is estimated to be 1.44 mg of ammonia per day. A 50 kg person would therefore be exposed to 0.024 mg of ammonia per kg of body weight. The LD_{50} is more than 14,000 times the ammonia exposure for a two-pack-a-day CAMEL Filter smoker.

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Inhalation Toxicity

Ammonia is a respiratory irritant and inhalation in high concentrations may cause edema of the respiratory tract, fit of glottis and suffocation. The lethal concentration in cats (LD_{50}) was determined to be 10,000 ppm for one hour.

Comparison of Smoker Exposure to Threshold Limit Value Exposure

Because of the extensive use of ammonia in commercial processes such as in the manufacture of fertilizer, nitric acid, hydrazine hydrate, nitriding of steel, etc., the safe exposure levels for workers in industry have been thoroughly investigated. As a result of these investigations, Threshold Limit Values for ammonia exposure have been established. It is of interest to compare the level of exposure permitted for ammonia in the work place to the level of exposure for a two-pack-a-day CAMEL Filter smoker.

According to the ACGIH recommendations, the Threshold Limit Value (TLV) for ammonia is 18 mg/m³ of air. It is estimated that the average person inhales 10 m³ of air in an eight-hour period (International Commission on Radiology Protection: Report of Task Group on Reference Man, Pergamon Press). During an eight-hour work day, a person working in an atmosphere containing 18 mg of ammonia per cubic meter of air would inhale 180 mg of ammonia. This is 125 times the estimated daily dose for a two-pack-a-day CAMEL Filter smoker.

These two types of exposure may not be comparible because the occupational exposure is spread over an eight-hour day, and the cigarette exposure occurs during irregularly spaced intervals throughout the day. According to ACGIH regulations, a short-term exposure limit (less than 15 minutes) to ammonia at 27 mg/m³ is permissible. A person working in an atmosphere containing 27 mg of ammonia per cubic meter of air would inhale 5.4 mg of ammonia in 15 minutes. This is over 200 times the amount of ammonia a smoker would inhale if he or she smoked one CAMEL Filter cigarette every 15 minutes.

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R.J. Reynolds Tobacco Co.

RJR

Dr. G. R. DiMarco

Attached are position papers describing our rationale for using the following additives in RJRT tobacco flavor formulations:

Ammonia

Glycerol

Sclareolide

Sucrose Tetraisovalerate

Based on our discussion on July 16, 1982, we did not prepare a position paper on Coumarin.

Whether you and Dr. Colberg have had an opportunity to review the papers, we would like to discuss what additional information will be required.

E. Bernasek

C. W. Nystrom

HUMAN USE

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BJG Exhibit 1094
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DRAFT 8-9-52

AMMONIA

Ammonia is used by RJRT in the following tobacco processing operations.

(1) Denicotinization of burley tobacco

(2) Ammoniation of reconstituted tobacco

Denicotinization of Burley Tobacco

Denicotinization of some of our burley tobacco gives us greater flexibility in the types of tobacco we can use in our products to meet the constantly changing demands by consumers for cigarette products with different tar and nicotine levels. This process also permits us to partially or completely compensate for the year to year variation in the nicotine content of burley tobacco.

In the denicotinization process, burley tobacco is first treated with gaseous ammonia, and then contacted with steam to remove nicotine and excess ammonia. In this space the major portion of the nicotine in the tobacco is present as nicotine salts (citrate, oxalate, malate), the major portion of the calcium ammonia is present in the form of the ammonium salts of the acids.

Denicotinization produces the following changes in chemical composition of burley tobacco and smoke: (1) decreased nicotine content of the tobacco; (2) decreased levels of nicotine, related alkaloids, pyrazines and pyridines in the smoke, (3) increased ammonia content of the tobacco; and (4) increased level of ammonia in the smoke.

The magnitude of some of the chemical changes that occur in burley tobacco and smoke are shown in Table I. These data were taken from a report by C. R. Green et al., RSK, 1954, No. 3.

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TABLE I

EFFECT OF PY PROCESSING ON BURLEY[a] SMOKE AND TOBACCO COMPOSITION

Analysis	L9120A	L9120B	% Difference	L9769A	L9769B	% Difference[b]
Smoke[c]						
TPM, mg	35.0	33.0	ND[d]	37.4	31.9	-15
TPM water, mg	4.3	3.9	ND	4.9	3.7	-24
Nicotine, mg	4.17	1.80	-57	5.22	1.79	-66
FTC "tar", mg	26.5	27.2	ND	27.4	26.5	ND
Puffs	8.9	8.9	ND	9.1	9.0	ND
pH, Average	7.08	7.08		7.08	6.55	
Average	8.71	8.61		7.89	8.24	
Carbon monoxide, mg	15.4	17.6	14	19.0	19.4	ND
Formaldehyde, ug	49	55	ND	105	103	ND
Acetaldehyde, ug	935	835	ND	935	930	ND
Acrolein, ug	81	69	-15	93	82	-12
Ammonia, ug	87	178	105	123	251	104
Hydrogen cyanide, ug	297	279	ND	314	322	ND
Nitrogen oxides, ug	712	752	ND	814	819	ND
Isoprene, ug	835	490	-41	560	470	-13
Phenol, ug	95	81	-15	103	113	ND
3-Deoxyglucopyranose, ng	11.2	10.7	ND	-	-	-
Weight, g	1.111	1.074				
PD, Inches Water	2.45	2.62				
Sugars, %	1.7	1.4	-17			
Nicotine, %	3.22	1.24	-61			
Ammonia, %	0.70	0.82	17			

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[a]Control Burley = LN120A or LN795A Test Burley = LN120B or LN795B

[b]% Difference = 100 (A-B)/B where A = Test Burley value, B = Control Burley value

[c]Value per cigarette

[d]ND = No difference; values fall within ± 10%

[e]Nitrogen oxides are expressed as NO_2

RJR is currently using 5-12 percent denicotinized burley tobacco, based on the total blend, in all brands except the MORE family. The MORE brands contain 19-24 percent denicotinized burley tobacco based on the total blend.

Ammoniation of Reconstituted Tobacco

Studies on the ammoniation of reconstituted tobacco were started in 1973 as a result of [illegible] studies carried out during the 1950's and early 1970. During the 1950's, [illegible] Jr. investigated the ammoniation of tobacco and tobacco sheets and reported dramatic improvements in the smoking qualities of ammoniated tobacco. Smoke harshness and irritation were reduced and taste properties were improved.

In the early 1970's, a major R&D program was initiated to investigate the physical chemistry of tobacco and tobacco smoke in an attempt to gain a better understanding of the factors influencing smoke harshness, irritation and strength. These studies led to the following observations and conclusions.

(1) The pH of cigarette smoke is important to smoke quality and can be used as a measure of the physiological strength of smoke.

(2) Ammonia in smoke is one of the major pH controlling components. Others include nicotine, amines, organic acids and carbon dioxide.

(3) Ammonia occurs naturally in tobacco ranging from trace amounts in flue-cured tobacco to over 1 percent in high quality cigar tobaccos.

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(4) Philip Morris introduced the use of added ammonia in their cigarette products in 1955. They use diammonium hydrogen phosphate in their reconstituted tobacco process to liberate ammonium bicarbonate prior to casting a reconstituted tobacco sheet (RDH, 1972, No. 10).

(5) Philip Morris brands, especially Marlboro, began growing in sales very rapidly after the introduction of added ammonia.

(6) Correlation studies relating increased smoke pH to sales trends show a very strong positive correlation (RDH, 1973, No.17).

(7) Studies of the effect of ammonia on smoke composition showed a reduction in aldehydes, especially formaldehyde, and an increase in levels of pyridines, pyrazines, and minor alkaloids. Smoking results showed a decrease in smoke irritation and harshness and an increase in physiological satisfaction with increasing ammonia content.

Based on the above observations, it was decided to investigate the use of ammoniated reconstituted tobacco (C7A) as a means of increasing the smoke pH of Kent's cigarette products. ISO tests indicate that smokers prefer products containing C7A over products containing only C7 (untreated reconstituted tobacco). Since the introduction in CAMEL Filter in 1975, C7A has been tested and/or introduced in nineteen additional brands.

Analytical data show that the current CAMEL Filter, which contains both ammoniated tobacco (7.6 percent based on total blend) and C7A (27.5% percent based on total blend), delivers approximately 35 ug of ammonia per cigarette in the mainstream smoke. A two-pack-a-day CAMEL Filter smoker will be exposed to approximately 1870 ug of ammonia per day.

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BIOLOGICAL DATA ON AMMONIA

[redacted] catabolic and metabolic processes. Excess amounts of ammonia produced in the body are converted to [redacted] and excreted as urea in the urine.

Ammonia or its salts are natural components of many of our foods. Also, a number of ammonia-containing compounds are considered GRAS when used as miscellaneous and/or general purpose food additives. These include ammonium hydroxide, ammonium bicarbonate, ammonium carbonate, ammonium saccharin, ammonium sulfate and ammonium phosphate. Other specific applications permit the use of ammonium caseinate, ammonium chloride, ammonium isovalerate, ammonium persulfate, ammonium sulfide, ammonium sulfite, etc. in food products.

Clearly, the use of ammonia in the processes described in this paper are similar to many of the applications commonly used in the food industry. Hence, there would be little reason to expect any undesirable effects.

Although the total ammonia in tobacco smoke can be determined, the actual form of the ammonia is probably as the salts of carbonic acid, isovaleric acid, and other organic acids. Ammonia salts of acids, with the exception of the salts of strong acids such as hydrochloric and sulfuric acid, are usually less irritating and less toxic than free ammonia. Therefore, if we compare the level of total ammonia in cigarette smoke with the known biological effects of ammonia, we are no doubt overestimating any effect.

Acute Toxicity

The acute oral toxicity (LD_{50}) of ammonia in rats is 350 mg/kg body weight. Maximum exposure for a two-pack-a-day CAMEL Filter smoker is estimated to be 1.44 mg of ammonia per day. A 50 kg person would therefore be exposed to 0.029 mg of ammonia per kg of body weight. The LD_{50} is more than 12,000 times the ammonia exposure for a two-pack-a-day CAMEL Filter smoker.

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The Health Consequences Of Smoking: CARDIOVASCULAR DISEASE

The Health Consequences Of Smoking

CARDIOVASCULAR DISEASE

a report of the Surgeon General

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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The Health Consequences Of Smoking

CARDIOVASCULAR DISEASE

a report of the Surgeon General

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THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

NOV 17 1983

TO THE READERS OF THIS VOLUME:

Provisions of the Public Health Cigarette Smoking Act of 1969 (P.L. 91-222) require the Secretary of Health and Human Services to submit an annual report to the Congress on the health consequences of smoking. Attached is the 1983 report, Health Consequences of Smoking: Cardiovascular Disease. This volume is an in-depth analysis of the scientific evidence of the relationship between cigarette smoking and multiple cardiovascular diseases. This relationship is quantitatively the most serious of the health consequences of smoking, but is poorly recognized by the public.

This report represents the consolidated work of many widely-recognized experts known for their contribution to understanding cardiovascular disease. It is a scientific reference document to serve as a state-of-the-art source for medical and behavioral scientists and researchers.

Smoking-related cardiovascular disease is estimated to account for more deaths than any other smoking-related disease, including cancer. This report clearly establishes that cigarette smoking increases the risks for a number of cardiovascular diseases, particularly coronary heart disease, the largest single cause of deaths in the United States. In addition, smoking is related to an increased risk for stroke, atherosclerosis, and other circulatory diseases.

The report clearly demonstrates that cigarette smoking is a major risk factor for coronary heart disease in the United States. There are 55 million persons who smoke, a larger population than those who have hypertension or elevated cholesterol, the other major risk factors for this disease. Smokers' death rates from coronary heart disease are 70 percent greater than those of non-smokers. Simply by quitting smoking, these men and women dramatically reduce their risk of premature death from this disease.

The economic and social toll these smoking-related deaths extract from the Nation's health is immeasurable. The report's findings re-emphasize the importance of this Department's continued educational efforts to enable a fully-informed choice by individuals on whether to begin or to continue to smoke.

In my view, this volume is a solid scientific work and a contribution to the prevention efforts of this Department.

Margaret M. Heckler

Margaret M. Heckler
Secretary

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FOREWORD

The 1983 Report is the second volume in *The Health Consequences of Smoking* series that focuses on specific diseases. The 1982 Report reviewed in depth the association between tobacco use and various cancers; the 1983 Report is a comprehensive review of the relationship between smoking and cardiovascular disease.

The ability to draw a conclusion from the scientific evidence on the causal relationship between smoking and cardiovascular disease was reached more recently than it was from the evidence on the relationship between smoking and cancer. The latter relationship was first established scientifically 30 years ago, particularly for lung cancer. At the time the Advisory Committee on Smoking and Health was formed in 1962, the scientific evidence linking tobacco use, particularly cigarettes, with respiratory cancers was overwhelming. A causal link between cigarette use and lung cancer was both clear and compelling. A number of epidemiological studies on the relationship between smoking and coronary heart disease (CHD) existed at that time, but the Committee felt that the evidence was insufficient to make a judgment of a causal relationship.

Nevertheless, the Committee found the evidence compelling enough to caution that even though the causal role of cigarette smoking in coronary heart disease was not proved, countermeasures were warranted, and the Committee counseled against postponing action until no uncertainty remained. The evidence was reviewed again in the 1971 Surgeon General's Report and was, by this time, clearly strong enough to establish cigarette smoking as a major risk factor for coronary heart disease in men. By 1979, when the 15th year anniversary Report of the Surgeon General was published, there was no longer any doubt that cigarette smoking was directly related to coronary heart disease for both men and women in the United States.

The Importance of Cardiovascular Disease

The importance of cardiovascular disease, particularly coronary heart disease, to the health of the American public is evident. In 1980 cardiovascular disease accounted for approximately half of all U.S. deaths—960,000 out of 1,980,000 total deaths. Of these, slightly

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over 565,000 were due to coronary heart disease; that is, approximately 30 percent of all deaths and almost 60 percent of all cardiovascular deaths were due to CHD. The age-adjusted CHD death rate peaked in 1963 and by 1980 had declined 30 percent. In the period between 1968 and 1978 alone, the age-adjusted rate declined 26.5 percent, with a greater decline noted for the younger age groups.

In comparison, the total number of all cancer deaths was slightly over 416,000 in 1980. Thus, deaths from CHD exceeded all cancer deaths, and deaths from all cancers numbered less than one-half the total of all cardiovascular deaths.

Last year this Department issued a report in which it was estimated that tobacco use, particularly cigarette smoking, was related to 30 percent of all cancer deaths in the United States—a projected 129,000 premature deaths. The findings of this year's Report, however, should be considered even more alarming, in that the number of cardiovascular deaths that are reasonably estimated to be cigarette related is even higher. A number of investigators[1] have estimated that 30 percent, or more, of CHD deaths could be attributed to cigarette smoking because of the higher CHD death rates experienced by eversmokers compared with neversmokers. If 30 percent of coronary heart disease deaths are attributed to cigarette smoking, 170,000 Americans will die prematurely of CHD each year. Smokers also experience increased death rates owing to other cardiovascular diseases such as stroke, peripheral vascular disease, aortic atherosclerosis, and other vascular problems.

Findings of the 1983 Report—Coronary Heart Disease and Cigarette Smoking

Each of the three major risk factors poses approximately the same increase in risk of CHD for the person with the risk factor, but cigarette smoking is far more prevalent as a risk factor for CHD in the American population than either hypertension or elevated serum cholesterol. Thus, the overall finding of this Report is clear: **Cigarette smoking should be considered the most important of the known modifiable risk factors for coronary heart disease in the United States.**

For over 25 years, cigarette smoking has been linked epidemiologically with an increased risk of dying from coronary heart disease. As early as 1954, a strong, statistically significant association between cigarette use and CHD was demonstrated. In the intervening years, additional studies have confirmed this association. An examination of only the major prospective studies, involving more than 20 million person-years of observation, indicates that smoking has been consistently shown to elevate CHD mortality rates. Overall, smokers have a 70 percent greater CHD mortality than nonsmokers. Heavy smokers, those who consume more than two packs per day, experience CHD mortality rates almost 200 percent greater than nonsmokers.

In the National Pooling Project study, a unique study that combined data from five of the Nation's largest incidence studies on heart disease, smokers of a pack or more per day were found to have a greater than 2.5-fold increased risk of developing a major coronary event compared with nonsmokers. This study also found that smokers who have other major risk factors experience a greater increased risk than would be expected from the summation of the independent risks. Thus, cigarette smoking interacts with the other major risk factors in a manner that greatly increases the risk of CHD.

The risk of developing and dying from CHD is directly related to the total dosage of cigarette smoke exposure. A dose-response relationship has been established for the number of cigarettes smoked per day, the total years of cigarette smoking, and the degree of inhalation; CHD risk is inversely related to the age of initiation. CHD mortality ratios are also greater at the younger age groups; thus, preventive efforts could truly have a decided impact on extending life-expectancy—if large numbers of smokers could be persuaded to quit smoking. The decrease in elevated CHD risk with cessation, coupled with the prevalence of smoking as a risk factor in the U.S. population, means that the elimination of cigarette usage could have a greater impact on CHD morbidity and mortality than any other preventive measure.

Sudden Cardiac Death

Smokers are at a two to four times greater risk for sudden cardiac death (SCD) than are nonsmokers. The risk for sudden death increases with increasing daily exposure, as measured by the number of cigarettes consumed per day.

Stroke

The association between cigarette smoking and cerebrovascular disease (CVD) is largely confined to the younger age groups, with little evidence of an effect after age 65. The number of stroke deaths in 1980 totaled 170,000; even a small percentage of such deaths represents thousands of premature deaths.

[1] Report of the Royal College of Physicians, London, 1976; Hammond and Horn, Journal of the American Medical Association, 1958; Doll and Hill, British Medical Journal, 1964; Kahn, Journal of Chronic Diseases, 1966; Rogot and Murray, Public Health Reports, 1980; Garfinkel, Proceedings of the Fourth World Conference on Smoking and Health, Stockholm, 1969. See Section 3 for additional discussion.

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Women

For women who both smoke cigarettes and used oral contraceptives, a strong association exists between their use and one form of stroke—subarachnoid hemorrhage. Smoking and oral contraceptive use appear to interact synergistically to greatly increase the risk of subarachnoid hemorrhage and of CHD, compared with the risk for those women who neither smoke nor use oral contraceptives.

Other Cardiovascular Disease

Cigarette smoking contributes to the development of aortic atherosclerosis and arteriosclerotic peripheral vascular disease (APVD). Ninety percent of patients with APVD are cigarette smokers, and the successful management of this disease includes complete smoking cessation by such patients.

Changing Trends in Smoking Behavior and Coronary Heart Disease

Demographers have noted a reduction in mortality rates from heart disease for several years. However, a sharp decline in these rates occurred in the late 1960s for reasons that are not entirely known. Significantly, declines in cigarette smoking prevalence among adults were first noted in 1964, the year of the first Surgeon General's Report, with declines in prevalence accelerating between 1966 and 1970. By 1980, overall adult smoking prevalence had declined by nearly 25 percent. While the magnitude of the impact of these changes in smoking behavior on the decline in CHD death rates is uncertain, the direction and nature of that impact is not. The substantial changes in smoking behavior that have occurred over the last 20 years have exerted, and will continue to exert, a substantial beneficial effect on the incidence of CHD in the U.S. population.

We know from cohort mortality studies, incidence studies, and, more recently, intervention trials that smoking cessation results in a reduction in CHD mortality.

Data from the Multiple Risk Factor Intervention Trial (MRFIT) have shown that those cigarette smokers who reported quitting at their first-year interview (after an average of 6 years of followup) reduced their relative risk for CHD mortality by almost half compared with those smokers who continued to smoke. Mortality from all causes was almost 30 percent lower among those who quit smoking compared with those who continued to smoke. These data correlate well with those observed in the cohort mortality studies, which have consistently shown a decline in CHD mortality among former smokers compared with continuing smokers. In some studies a substantial improvement in mortality within the first few years after smoking cessation was demonstrated.

Public Perception of the Scientific Link Between Cigarette Smoking and CHD

A recent staff report by the Federal Trade Commission revealed that a substantial proportion of the American public is not aware of the link between cigarette smoking and heart disease. When asked to respond to the statement "Cigarette smoking is a major cause of heart disease," 40 percent of adults responded "false" or "don't know," including almost half of the adult smokers (45 percent). This concurs with results from a 1980 Roper survey, which found that 53 percent of the population and 58 percent of smokers did not know that smoking causes *many* cases of heart attack; a surprising 20 percent were not even aware that smoking causes *some* cases.

It is apparent that for a significant segment of the general public, a large gap exists in its understanding of the relationship between cigarette smoking and heart disease, a relationship that accounts for the largest number of excess deaths of all the diseases associated with cigarette smoking.

In last year's Report, I stated that the education of our citizens regarding the health hazards of smoking cannot be left solely to government. The findings of this Report and previous ones compel me again to ask for an increased commitment by the health care community, voluntary health agencies, schools, and other groups in our society to join this Department and the Public Health Service in our continuing efforts to reduce the premature death and disability associated with cigarette smoking through renewed efforts of education and information.

Edward N. Brandt, Jr., M.D.
Assistant Secretary for Health

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PREFACE

In 1982, the Public Health Service's Report on the health consequences of smoking dealt with the relationship between smoking and cancer. This 1983 Report turns its attention to the relationship between cigarette smoking and cardiovascular disease, one that imposes an even greater burden of disease and premature death.

In preparing this Report, the Public Health Service has reviewed a world literature that goes back more than 40 years and has examined the results of epidemiological observations covering many millions of person-years. This evidence permits us to affirm again what was said in our 1979 Report and what is the consensus of other scientific bodies here and across the world. Cigarette smoking is causally related to heart disease; it and elevated levels of serum cholesterol and hypertension constitute the major risk factors for contracting and dying from this disease.

Since 1979, much additional information has accumulated to support this judgment. From a public health viewpoint, the most important is the new and further evidence presented in this volume that when one quits smoking, the risk of dying from heart disease begins to recede almost immediately and eventually becomes no greater than that experienced by someone who has never smoked at all. This is an encouragement to personal action and a justification for much greater research and program effort by government and voluntary agencies in helping people to quit smoking.

As in all previous Reports, the Public Health Service has turned to many people and agencies within the research and clinical community in developing this statement. On behalf of the Service, I express my respect and gratitude to them.

C. Everett Koop, M.D.
Surgeon General

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52649 4547

TABLE OF CONTENTS

Foreword iii

Preface ix

Acknowledgements xi

1. Introduction, Overview, and Conclusions 1

2. Arteriosclerosis 13

3. Coronary Heart Disease 63

4. Cerebrovascular Disease 157

5. Atherosclerotic Peripheral Vascular Disease and Aortic Aneurysm 177

6. Pharmacological and Toxicological Implications of Smoke Constituents on Cardiovascular Disease 203

7. Changes in Cigarette Smoking Behavior in Clinical and Community Trials 241

8. The Effect of Cigarette Smoking Cessation on Coronary Heart Disease 291

A. Trends in Cardiovascular Diseases 327

B. Trends in U.S. Cigarette Use, 1965–1980 361

Index 375

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SECTION 5. ATHEROSCLEROTIC PERIPHERAL VASCULAR DISEASE AND AORTIC ANEURYSM

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Atherosclerotic Peripheral Vascular Disease

Introduction

The peripheral arteries include those branches of the aorta supplying the upper and lower extremities and the abdominal viscera. Most peripheral arterial occlusive disease is due to atherosclerosis, although other conditions such as fibromuscular dysplasia, muscular entrapment, cystic adventitial degeneration, and arteritis may cause obstruction of the peripheral arteries. Symptomatic atherosclerotic peripheral vascular disease (ASPVD) occurs most often in the vessels of the lower extremities. The anatomic location of such disease is usually classified according to the major arterial segments involved, including aortoiliac, femoro-popliteal, and tibio-peroneal artery occlusive disease. Occlusive lesions of the origins of visceral arteries commonly involve the renal arteries and the mesenteric arteries, including the celiac and superior and inferior mesenteric arteries.

With many asymptomatic patients, peripheral arterial occlusive disease can be detected on physical examination. Symptomatic patients are usually classified according to the severity of presenting complaints; for example, patients may be classified as suffering intermittent claudication (leg pain brought on by exercise and relieved by rest), ischemic rest pain, or, the most severe complaint, tissue necrosis, including gangrene or ischemic ulceration. Patients with renal artery occlusive disease may present with severe and uncontrollable hypertension, although such patients may respond to medical treatment for hypertension. Patients with arterial occlusive disease of the mesenteric arteries may present with acute ischemia of the intestine, due to thrombosis or embolization, or with more chronic symptoms of pain aggravated by eating and weight loss.

The diagnosis of peripheral arterial occlusive disease can usually be made from the history and physical examination, including the evaluation of peripheral arterial pulsations and detection of arterial bruits. However, more accurate and objective diagnosis of peripheral arterial occlusive disease is possible with noninvasive diagnostic techniques, particularly Doppler ultrasound or plethysmography. Arteriography is reserved for patients with symptoms sufficient to make them candidates for surgery, and is not usually required for the diagnosis of peripheral arterial occlusive disease.

The majority of patients with peripheral arterial disease may be candidates for medical therapy such as exercise regimens and reduction of known risk factors through cessation of smoking, control of diabetes mellitus, dietary measures to control hyperlipidemia and obesity, and medical management of hypertension. Intensive foot hygiene and avoidance of trauma are additional important medical measures for patients with lower extremity ASPVD. The

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newly developed treatment of balloon dilatation (percutaneous transluminal angioplasty) may be used to restore pulsatile flow for severely symptomatic patients. Surgical therapy is required in only about 10 percent of the patients with advanced arterial occlusive disease. One surgical approach is arterial reconstruction, usually involving endarterectomy or bypass with vein or prosthetic grafts of diseased segments. Sympathectomy is infrequently used, but it may be helpful in patients with cutaneous ischemia, for whom restoration of pulsatile flow is not possible. Amputation of limbs with advanced arterial occlusive disease that cannot be remedied by surgical reconstruction remains in use, but it is required by only about 5 percent of all patients presenting with peripheral arterial occlusive disease.

Risk Factors for Peripheral Arterial Occlusive Disease

The most powerful risk factor predisposing to atherosclerotic peripheral arterial occlusive disease is cigarette smoking (*47*); in fact, the rarity of peripheral arterial occlusive disease in patients who have never smoked was noted by Eastcott as early as 1962 (*23*). The epidemiologic evidence linking cigarette smoking to atherosclerotic peripheral arterial occlusive disease is discussed in detail below.

Several studies have suggested hyperlipoproteinemia as a risk factor contributing to atherosclerotic peripheral arterial occlusive disease. The type of hyperlipoproteinemia and the degree of association with peripheral vascular disease appear to be different, however, from the hyperlipoproteinemia associated with coronary artery disease. Zelis et al. (*92*) reported that patients with Type III hyperlipoproteinemia are particularly susceptible to the development of peripheral vascular disease, and they noted objective improvement in the peripheral circulation with medical treatment of this disorder. Greenhalgh et al. (*30*) reported that fasting serum lipid concentrations were abnormally high in 44 percent of a consecutive series of 116 patients with proven peripheral vascular disease. In 39 percent of the patients the serum triglyceride level was raised, and in 15 percent the serum cholesterol level was increased. Ballantyne and Laurie (*5*) evaluated 353 consecutive patients with peripheral vascular disease and showed a predominance of Type IV hyperlipoproteinemia in males, but a predominance of Type IIa hyperlipoproteinemia in females. Patients with peripheral vascular disease and Type IIa or Type IIb hyperlipoproteinemia were more likely to have associated coronary artery disease. Eighty-four percent of the patients were cigarette smokers, with the majority smoking more than 10 cigarettes daily. There was no relationship between cigarette consumption and the occurrence of hyperlipoproteinemia. However, Farid et al. (*25*) found that in 122 patients with angiographically proved peripheral arterial occlusive disease, heavy smoking seemed to be associated with an unexpectedly high proportion of an abnormal lipid pattern: 43 percent of the males exhibited Type IV hyperlipoproteinemia. Lawrie et al. (*51*) surveyed 4,477 healthy males and females in the west of Scotland and found a high prevalence of hyperlipoproteinemia of Type II and Type IV. Hyperlipoproteinemia occurred more frequently in survivors of myocardial infarction, but also occurred, though to a lesser extent, in patients with peripheral vascular disease.

Olsson and Eklund (*57*) evaluated 160 men and 123 women with digit plethysmoraphy and found that most atherogenic lipoprotein abnormalities associated with disease of the lower extremities involved the relatively triglyceride-rich part of the low density lipoprotein (LDL) fraction and the relatively cholesterol-rich part of the very low density lipoprotein (VLDL) fraction. These authors found a deleterious influence of smoking even in the preclinical stage of peripheral vascular disease. Davignon et al. (*18*) evaluated 114 French Canadian patients with angiographically proved peripheral vascular disease. The severity of atherosclerosis correlated positively with plasma triglyceride concentration, but cigarette smoking was the risk factor most frequently found in patients with peripheral vascular disease. In contrast, Erikson et al. (*24*) did not find a positive correlation between arteriographic changes in 30 patients with intermittent claudication and serum concentrations of lipids and lipoproteins. Trayner et al. (*80*) compared 32 patients with peripheral vascular disease to control subjects. The vascular disease study group had a significantly higher incidence of hypertriglyceridemia, more marked for the males, and had lower levels of high density lipoproteins (HDL) than did the control subjects. The study group also had a twofold higher prevalence of cigarette smoking than control subjects. Control patients who smoked also had lower levels of HDL than those who did not smoke. Phillips et al. (*61*) also established a relationship between an increase of VLDL triglyceride and cigarette smoking, while HDL cholesterol decreased with cigarette smoking.

Hypertension is associated not only with coronary and cerebrovascular disease, but also with peripheral arterial occlusive disease (*46*). Larson et al. (*50*) established an interaction of hypertension and hypercholesterolemia in an experimental study of mongrel dogs, suggesting that the combination of these two risk factors produces alterations in lipid composition in the canine aorta that appears to be geometric rather than arithmetic in nature. However, Stehbens (*74*) claimed that epidemiologic studies are less conclusive than experimental studies in establishing the relationship of risk factors in atherosclerosis. He postulated that local hemodynamics associated with hemodynamic stress, rather than the level of lipid intake, is the

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principal factor governing the accumulation of lipid in the vessel wall.

It is clear that multiple risk factors have been associated with atherosclerosis not only in the coronary and cerebrovascular arterial beds but also in the peripheral circulation. Rosen et al. (65) evaluated the association of risk factors in 109 patients with peripheral arterial occlusive disease. The arterial disease was established by clinical and arteriographic examination and classified into three anatomic groups—aortoiliac, combined aortoiliac and femoropopliteal, and femoropopliteal disease. Type IV hyperlipoproteinemia and glucose intolerance were significantly more common in patients with isolated femoropopliteal disease. Cigarette smoking was the most prominent risk factor in all groups, occurring in 90 percent of patients with aortoiliac or combined disease and in 75 percent of patients with femoropopliteal artery disease. The onset of clinical symptoms occurred at an average of 8 to 10 years earlier in smokers than in nonsmokers. Heyden et al. (35) established that smoking and coffee drinking interact in affecting LDL and total cholesterol, but coffee drinking alone did not appear to affect blood lipids. Criqui et al. (16) reviewed the relationship between cigarette smoking and HDL cholesterol in 2,663 men and 2,553 women aged 20 to 69 years in 10 North American populations of the Lipid Research Clinics Program Prevalence Study. Cigarette smoking was associated with substantially lower levels of HDL cholesterol; this association was dose related. Hulley et al. (37) found the same association in a longitudinal study of 301 high-risk males 35 to 57 years of age. After 1 year's intervention on diet, hypertension treatment, and smoking counseling, both smoking frequency and serum thiocyanate were significantly and independently associated with the changing plasma HDL-cholesterol concentration. A relationship linking cigarette smoking and abnormal lipoprotein metabolism comes from the report of Topping et al. (78), which found that patients with both Type III hyperlipoproteinemia and cigarette smoking suffer abnormalities of liver metabolism of cholesterol-rich "remnants." Such impaired hepatic metabolism may result in hyperlipoproteinemia and subsequent peripheral vascular disease.

Summary of Epidemiologic Studies

Because peripheral arterial occlusive disease does not pose as severe a mortality threat as coronary artery disease does, there have been fewer major epidemiologic studies of peripheral vascular disease. However, the underlying pathologic lesion, atherosclerosis, remains the same in the two conditions, and there is increasing evidence of an association between peripheral vascular disease and similar lesions in the coronary or cerebrovascular beds. Both clinical and angiographic correlates of peripheral arterial disease with concomitant coronary artery disease were suggested by the reports of Friedman et al. (23), Kannler et al. (49), Silvestre et al. (72), and Hertzer et al. (34). These reports not only suggest a clinical relationship between peripheral and coronary artery occlusive disease, but also indicate that the perioperative and long-term risks of treatment for peripheral vascular disease are strongly influenced by the presence of concomitant coronary artery disease.

Several publications have extensively reviewed the evidence associating cigarette smoking with peripheral arterial occlusive disease (81, 82, 83). Early studies by Juergens et al. (44), Begg (7), Schwartz et al. (71), and Widmer et al. (87) documented a much higher prevalence of cigarette smoking (usually exceeding 90 percent) in patients with peripheral arterial occlusive disease, when compared with control patients without vascular disease. Data from the Framingham study (46) suggest that cigarette smoking is one of the major risk factors in the development of intermittent claudication (Table 1). Over a 16-year period of followup, a higher total incidence and a higher annual incidence of intermittent claudication were noted in smokers as compared with nonsmokers. This difference was statistically significant for all age groups of both sexes. Using multivariate analysis to control for other risk factors, this relationship of smoking to intermittent claudication became stronger.

Many other investigators have noted a high prevalence of cigarette smoking in patients with peripheral arterial occlusive disease. Tomatis et al. (77) found that 98 percent of patients with aortoiliac disease and 91 percent of patients with femoropopliteal disease were cigarette smokers. Astrup et al. (3) found a significant correlation between the frequency of severe intermittent claudication and the consumption of more than 15 cigarettes a day in nondiabetic patients with peripheral vascular disease. A significant difference between heavy smokers and other smokers was not found, however, for the development of gangrene. Further, the development of claudication did not vary with the number of years of smoking or the total number of cigarettes consumed in a lifetime. Weinroth and Herzstein (84) noted a 50 percent greater incidence of peripheral arterial occlusive disease in diabetics who smoked than in those who did not. Juergens et al. (44) followed 520 patients with nondiabetic peripheral arterial occlusive disease, approximately 50 percent of whom continued to smoke despite medical advice to quit. Of those who continued to smoke, approximately 10 percent eventually required amputation, but no amputations were necessary in patients who successfully stopped smoking.

Horowitz et al. (36) reported that age was a significant factor in the prevalence of arterial disease, with nearly half of the cases occurring in patients over the age of 70. A higher percentage of patients with

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TABLE 1.—Average annual incidence (over 16 years) of intermittent claudication according to cigarette habit at examination

Age at examination and cigarettes smoked per day	Men			Women		
	Subjects at risk[1]	Rate per 10,000		Subjects at risk[1]	Rate per 10,000	
		Actual	Smoothed[2]		Actual	Smoothed[2]
45–64 years	6290	16	15.9	7933	4	3.8
None	2342	6	9.8	4514	3	2.4
Under 20	903	17	13.4	1978	0	4.0
20	1496	30	18.3	1090	9	6.5
Over 20	1523	16	24.9	422	17	10.8
65–64 years	4494	51	51.3	5989	19	19.3
None	2170	28	27.6	4278	19	17.8
Under 20	743	61	43.6	1030	19	21.6
20	879	40	68.7	434	0	38.7
Over 20	670	127	107.9	197	76	33.1
65–74 years	1326	57	56.6	1924	31	31.2
None	790	44	55.2	1641	19	23.6
Under 20	354	96	57.3	209	94	46.3
20	167	90	59.5	79	0	88.5
Over 20	111	0	61.7	29	172	164.2

[1] Numbers of subjects at risk according to cigarettes smoked do not add to totals shown because some subjects are in the unknown category.

[2] The "smoothed" rates were based on the mean of the individual probabilities of development of intermittent claudication in the 2 years following examination, where individual probability is calculated according to cigarettes use at examination using the values of the parameters estimated by fitting the logistic function to the occurrence of intermittent claudication in the age group.

NOTE: The trend is significantly different from zero at the 0.05 level for women 65 to 74 years of age and at the 0.01 level for men 65 to 64.

SOURCE: Kannel and Shurtleff (49).

arterial disease smoked than did patients without arterial disease. A higher percentage of males than of females had peripheral arterial occlusive disease. De Backer et al. (*21*) likewise noted an increase in intermittent claudication with increasing age, but also found a significant correlation of serum cholesterol, systolic blood pressure, blood glucose, and cigarette smoking in patients with intermittent claudication.

Future epidemiologic studies of peripheral vascular disease must take into account the merits and limitations of the clinical diagnosis of peripheral arterial occlusive disease. Horowitz et al. (*36*) suggest that the judgment of trained paramedical personnel compares favorably with that of physicians in screening large numbers of patients for peripheral vascular disease.

De Backer et al. (*21*) emphasized the importance of using ankle systolic blood pressure measurement with Doppler ultrasound to objectively screen patients for peripheral arterial occlusive disease. Such useful techniques have been emphasized by Marinelli et al. (*54*) in a large epidemiologic study of vascular disease in patients with diabetes mellitus.

In addition to clinical studies, several autopsy surveys have reported an association between smoking and peripheral atherosclerosis (*59, 60, 66, 67, 75, 89*). Such studies have supported a direct association between smoking and the formation of abdominal aortic fatty streaks, as well as their subsequent conversion to raised lesions.

Most reports of peripheral vascular disease emphasize the predominant occurrence of this disorder in males (*88*). However, diabetes mellitus may predispose females to peripheral arterial occlusive disease in a frequency similar to that of males. Broome et al. (*12*) reported on 15 women with aortoiliac occlusive disease, all of whom were cigarette smokers (mean, 20 cigarettes a day), and none of whom had diabetes mellitus. The temporal trend toward increased smoking by women may significantly increase their risk of peripheral arterial occlusive disease. The Framingham heart study (*47*) found that the incidence of peripheral vascular disease was increased among smokers and that cigarette smoking was as strong an independent risk factor in women as in men. Heavy smokers had a threefold increase in the incidence of peripheral arterial occlusive disease. Weiss (*86*) evaluated 245 women with peripheral arterial occlusive disease. The risk in ex-smokers who had not smoked for 5 years or more was nearly normal, with a risk ratio of 1.06. Patients who had not smoked for 1 to 5 years had a risk ratio of 1.70. Patients who continued to smoke, but smoked less than one pack a day, had a risk ratio of 11.53, and those who smoked more than a pack a day had a risk ratio of 15.56. The risk for arterial occlusive disease was particularly associated with the proximal aortoiliac segment and was less associated with distal or femoral-popliteal artery disease. This study described both a dose–response effect and a benefit following cessation of smoking.

There have been few studies of the association of visceral arterial occlusive disease and cigarette smoking. Mackay et al. (*53*) reported on the correlation of smoking and renal artery stenosis. They found that smoking was nearly twice as common in patients with nonmalignant hypertension associated with renal artery stenosis as in those patients with hypertension of comparable severity without renal artery disease. Previous studies documented that a higher proportion of smokers was noted in patients with malignant hypertension (*10, 39*). Cigarette smoking was present in 20 of 22 patients with malignant hypertension and associated renal artery stenosis (*53*).

Cigarette smoking appears to be the only form of tobacco consumption associated with an increased risk of developing periph-

52649 4552

eral arterial occlusive disease. Smith (*73*) reported that no cases of intermittent claudication were found in patients who used only smokeless tobacco (snuff, chewing tobacco), provided that patients with a history of diabetes mellitus, heavy ethanol intake, or dietary problems were excluded.

Frishman (*29*) reviewed the effects of involuntary smoking on the cardiovascular system. Although levels of carbon monoxide commonly found in cigarette-smoke-filled environments have been demonstrated to decrease exercise tolerance in patients with existing angina pectoris and intermittent claudication, studies are not available to document the role that passive smoking might play in the etiology of atherosclerotic cardiovascular disease (*69*).

Clinical Investigations in Humans

In several studies, the effect of cigarette smoking or the constituents of cigarette smoke on the human peripheral vascular system has been investigated. Cryer et al. (*17*) studied the effects of cigarette smoking, sham smoking, and smoking with adrenergic blockade in 10 subjects. There was a significant increase in the mean plasma norepinephrine and epinephrine levels associated with smoking. The smoking-related increase in pulse rate, blood pressure, blood glycerol, and blood lactate-pyruvate ratio was prevented by adrenergic blockade. These findings were attributed to local norepinephrine release from adrenergic axon terminals within tissues rather than to increments in circulating catecholamines. In experiments comparing cigarettes of varying nicotine content, the subjective recognition of different cigarette brands may influence the results of clinical experiments. Ossip et al. (*58*) have suggested that nicotine extraction filters be used to minimize the within-subject differences due to the recognition of cigarette brand. The influence of the type of beta blocker used in therapy of patients who are cigarette smokers was investigated by Trap-Jensen et al. (*79*). These authors found that the use of a nonselective beta blocker, propranolol, during smoking caused a marked rise in diastolic and mean blood pressure and forearm vascular resistance, due to the blockade of adrenaline-induced vasodilatation, which is mediated by beta-2 receptors in the resistance vessels. Selective beta-1 blockade with atenolol attenuated the systolic blood pressure and the tachycardiac responses induced by cigarette smoking.

Several studies have suggested an association between cigarette smoking and the level of circulating hemoglobin. Castleden et al. (*14*) evaluated 61 male nondiabetic smokers with peripheral artery disease and compared them with age-matched nondiabetic male smokers and nonsmokers admitted for routine inquinal herniorrhaphy. They found a significant association between smoking and hemoglobin levels and a highly significant correlation between

smoking and peripheral vascular disease. In addition, the carboxyhemoglobin generated by smoking was associated with increased platelet adhesiveness, decreased fibrinolytic activity, and increased plasma fibrinogen. Yamori et al. (*91*) suggested that the hematocrit was increased in proportion to the number of cigarettes smoked and that this may be a mechanism for increased mortality rate from cardiovascular diseases in smokers.

Other hematologic effects of cigarette smoke have been observed in blood platelets and with fibrinolysis. Davis and Davis (*19*) studied 18 volunteers to assess the effect of cigarette smoking on platelet aggregation. The smoking of two unfiltered tobacco cigarettes during a 20-minute period resulted in a significant increase in the platelet aggregate ratio. During this time, the mean plasma nonesterified fatty acid concentration remained unchanged. These same authors (*20*) subsequently reported that the increase in the platelet aggregate ratio resulting from smoking two unfiltered cigarettes could be prevented with pretreatment with one aspirin tablet. Janzon and Nilsson (*43*) evaluated the fibrinolytic activity in vein walls among 71 randomly selected heavy smokers and 41 nonsmokers from a population of men born in 1914 residing in Malmö, Sweden. After 12 hours' abstention from tobacco, the smokers were found to have the same fibrinolytic activity as nonsmokers. Smoking six cigarettes during 3 hours increased the fibrinolytic activity in the blood, presumably because of the combined effects of nicotine and carbon monoxide.

Several studies of the effects of smoking on the peripheral circulation have involved noninvasive measurement of limb blood flow using plethysmographic techniques. Janzon (*40*) used a water-filled plethysmograph to study 71 randomly selected heavy smokers and 41 nonsmokers from the study group of men born in 1914 and residing in Malmö, Sweden. The smokers were found to have lower systolic and diastolic arm blood pressure and lower systolic blood pressure in the big toe with greater pressure gradients from the arm to the big toe compared with nonsmokers. During reactive hyperemia, smokers had decreased blood flow and increased peripheral vascular resistance. This same author (*42*) studied the acute effect of smoking on heart rate, blood pressure, and calf blood flow in 20 randomly selected 59-year-old male heavy smokers (more than 15 g of tobacco per day). After smoking two cigarettes, there was a significant increase in blood pressure and heart rate. Blood flow and resistance to blood flow in the calf did not change at rest, but during reactive hyperemia, the resistance to blood flow decreased and calf blood flow increased, an effect attributable to the peripheral vascular effects of nicotine. Janzon (*41*) evaluated 51 randomly selected 59-year-old heavy smokers for changes in peripheral vascular function after smoking cessation of 8 to 9 weeks. He noted an

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increase in blood flow during reactive hyperemia in patients who stopped smoking and a decrease in blood flow in patients who continued to smoke. Isacsson (38) performed venous occlusion plethysmography on the calf of 309 randomly selected 55-year-old men residing in Malmö, Sweden. Sixty-two percent of the total population examined were cigarette smokers. A history of intermittent claudication was present in 20 subjects, but arterial insufficiency could be clinically demonstrated in only 6 of the 20. Ilio-femoral occlusive disease was found in another eight patients. These patients had a higher prevalence of systolic hypertension, hypercholesterolemia, hypertriglyceridemia, and lipoprotein abnormalities. The amount of smoking was inversely related to the magnitude of the arterial flow capacity in the legs and directly related to the presence of occlusive arterial disease. More ex-smokers had high blood flow capacity than had a low flow capacity. The arterial flow capacity in the legs was reduced in direct proportion to the tobacco consumption per day. Coffman (15) used plethysmographic and isotope methods to document cutaneous vasoconstriction, increased skeletal muscle blood flow, and decreased venous distensibility in human subjects after tobacco smoking or nicotine injection.

Recent studies have employed Doppler ultrasound to document changes in blood velocity and transit time following cigarette smoking. Sarin et al. (68) noted a reduction in mean digital artery blood flow velocity of 42 plus or minus 6 percent following the smoking of a single cigarette in 10 male volunteers. Lusby et al. (52) evaluated the effects of cigarette smoking on hemodynamics in the large and small vessels of patients with peripheral arterial occlusive disease. Using Doppler probes, large vessel response to smoking was evaluated by measurement of pulse transit time delay. Patients with occlusive arterial disease had significant shortening in transit time delay, suggesting a stiffening in the main vessels in response to smoking. Such changes were not seen in control patients without peripheral arterial occlusive disease. A digit pulse volume recorder was used to measure the amplitude of digit pulsation, a measure of small vessel hemodynamics. The digit pulse amplitudes decreased significantly in response to both low and high nicotine cigarettes, and patients tended to self-titrate their nicotine intake. Due to this maintenance of nicotine level, the study failed to demonstrate a benefit on small vessel hemodynamics accompanying a switch from high to low nicotine cigarettes.

Recent studies suggest that tobacco allergy may play a role in the development of the cardiovascular effects of cigarette smoking. Becker and Dubin (6) reported that approximately one-third of healthy smoking and nonsmoking volunteers exhibited immediate cutaneous hypersensitivity to a glycoprotein antigen purified from cured tobacco leaves and found in cigarette smoke. Denburg et al. (22) skin-tested 164 peripheral vascular disease patients with purified tobacco glycoprotein. The authors also performed basophil degranulation tests to assess in vitro reactivity to tobacco glycoprotein. Immediate skin-test hypersensitivity to tobacco glycoprotein was found in 11 percent of patients with angiographically demonstrable peripheral vascular disease; a control group of normal patients was not skin tested. The basophil degranulation test was positive in 60 percent of smokers compared with 24 percent of nonsmokers ($p < 0.01$). Forty-three percent of skin-test-negative and 91 percent of skin-test-positive patients with peripheral vascular disease had a positive basophil degranulation test. Only 3 percent of patients with negative basophil degranulation tests had a positive skin test. The percent of patients with positive skin tests increased in proportion to the severity of angiographic peripheral vascular disease. What role tobacco hypersensitivity may play in the development of peripheral atherosclerosis remains to be elucidated.

A final area of clinical epidemiologic study is the relationship of maternal smoking to the fetal cardiovascular system. Asmussen (2) studied the umbilical artery, umbilical vein, and vessels of the placental villi of newborn children in relation to the maternal smoking history. His studies documented that severe damage to vessel walls is associated with maternal tobacco smoking during pregnancy. These fetal vascular changes may lead to vascular lesions later in life.

Experimental Studies in Animals

In several experimental animal studies, the relationship between cigarette smoking and atherosclerotic peripheral vascular disease has been investigated. Birnstingl et al. (9) evaluated the effect of short-term exposure to carbon monoxide on platelet adhesion in rabbits. In rabbits exposed on several occasions to an atmosphere containing 400 parts per million carbon monoxide for 6 to 14 hours, there was a highly significant increase in platelet stickiness immediately after exposure to carbon monoxide, followed the next day by a significant fall to levels below the preexposure value.

Richardson (62) evaluated the effects of nicotine and tobacco smoke on capillary blood flow in the rat. Red blood cell velocity in single capillaries within the mesenteric tissue of anesthetized rats was evaluated immediately before and after either intravenous injection of nicotine or inhalation of tobacco smoke. Blood velocity changes associated with tobacco exposure were considered to be passive consequences of changes in systemic arterial blood pressure. This study did not evaluate differential effects on various vascular beds of cigarette smoke or nicotine.

Fisher et al. (27) evaluated the effect of exposure of cholesterol-fed rabbits to the smoke of one cigarette daily over an 11- to 13-month

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period. The study failed to demonstrate quantitative or qualitative differences in atherosclerosis in the aorta or coronary or visceral arteries or significant changes in serum lipids. Boyce et al. (*27*) administered nicotine in the drinking water of New Zealand white rabbits during a 25-week period. Fasting serum levels of glucose, triglyceride, total cholesterol, and LDL cholesterol were elevated in the nicotine-treated rabbits compared with the controls. However, there was no significant difference between nicotine-treated and control animals in leukocyte, erythrocyte, and platelet counts or in hematocrit or hemoglobin. Endothelial cells from the aortic arch of nicotine-treated animals showed extensive changes, including increased cytoplasmic silver deposition, increased formation of microvilli, and numerous focal areas of "ruffled" endothelium (projections from the cell surfaces).

Marshall et al. (*55*) evaluated the effects in minipigs of exposure to cigarette smoke or varying concentrations of carbon monoxide for 1- to 16-hour periods. Cigarette smoke and short carbon monoxide exposure resulted in adherence of platelets to the endothelium. After longer exposures, microscopic thrombi were found in the vessel walls. Underlying degeneration in the endothelial cells developed upon exposure to carbon monoxide.

Recent investigations have involved the training of subhuman primates to smoke cigarettes in order to assess the effect on the peripheral circulation and hematologic factors. Schwartz et al. (*70*) have summarized data on experiments in baboons taught to smoke cigarettes. Rogers et al. (*63*) reported on 36 young adult male baboons who were fed an atherogenic diet. Twenty-eight baboons were randomly assigned to smoke 43 cigarettes daily, and 18 baboons were taught to puff air under equivalent experimental conditions. The cigarette-smoking baboons demonstrated significantly higher carbon monoxide and thiocyanate concentrations in blood and cotinine concentrations in the urine than did the nonsmoking baboons. There were no significant differences found in serum total cholesterol, VLDL, and LDL cholesterol or triglyceride concentrations in the smokers compared with the controls. Smoking baboons had significantly higher fasting glucose concentrations and lymphocyte counts. Platelet counts, platelet aggregation, food and water intake, and body weight were not significantly different in the two groups. Such experimental models may provide a valuable method to assess the long-term effects of smoking on the peripheral vascular system of primates.

Intervention Studies

There is considerable indirect evidence that cessation of smoking may significantly influence the effect of medical or surgical therapy on peripheral arterial occlusive disease. Unfortunately, the tendency of some patients with peripheral arterial occlusive disease to continue smoking often defeats the purpose of medical intervention. Thiruvengadam et al. (*76*) evaluated the effect of disease at different organ sites upon the smoking habit of chronic smokers. A significant reduction or cessation of smoking was observed in subjects with cardiovascular, pulmonary, neoplastic, or gastrointestinal disease, diabetes mellitus, or cirrhosis of the liver. Medical advice played a role in the reduction for only 19 percent of the subjects. Other reasons for reduction or cessation of smoking were socioeconomic factors, aggravation of disease, or belief in a possible relationship between smoking and the disease. Only subjects with psychiatric illnesses and peripheral vascular diseases showed no significant reduction in the smoking habit in comparison with the controls. Of 30 subjects with peripheral vascular disease, 12 increased their smoking with the advent of disease. Feinleib and Williams (*26*) emphasized that peripheral vascular disease risk is elevated only in cigarette smokers and not in cigar or pipe smokers. Smokers who quit gradually approach the lower risk of nonsmokers. Birkenstock et al. (*8*) reported on the role of cessation of smoking on the medical therapy of 390 patients with peripheral vascular disease who were either ineligible or unfit to undergo operative treatment. Conservative management included foot hygiene, walking exercise, cessation of smoking, a low cholesterol diet, and vitamin E therapy. Of 277 patients who smoked, 164 were able to stop smoking. Eighty-five percent of patients who stopped smoking showed improvement in symptoms of peripheral vascular disease on the medical regimen, in comparison with only 20 percent who improved among those who continued to smoke. The degree of improvement was greater in exsmokers than in nonsmokers. No patient with diabetes mellitus who continued to smoke improved under medical management.

Cessation of smoking appears to play an important role in the long-term success of reconstructive arterial surgery. Wray et al. (*90*) recorded a significantly higher rate of late arterial occlusion in patients who had undergone aortofemoral bypass and who persisted in smoking when compared with patients who stopped smoking postoperatively. In 30 patients who continued to smoke, 9 late occlusions occurred, but no occlusions developed in 16 patients who ceased smoking postoperatively. Myers et al. (*56*) reported a retrospective study of 217 patients undergoing aortofemoral (135) or femoropopliteal (107) vascular reconstruction. Patients who stopped smoking or smoked no more than five cigarettes daily after their operation had late patency rates of approximately 90 percent for aortofemoral reconstruction and 80 percent for femoropopliteal vein grafts. Patients who continued to smoke more than five cigarettes daily had a late complication rate approximately three times greater after aortofemoral reconstruction and four times greater after

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femoropopliteal vein grafting, compared with ex-smokers. The late patency rate was approximately inversely proportional to the number of cigarettes smoked per day after the operation. The incidence of late complications was not correlated with the number of cigarettes smoked prior to operation. Burgess et al. (*13*) noted that among patients whose below-knee amputation failed to heal, six of seven (85 percent) were cigarette smokers, whereas among those whose distal amputations healed, only half were smokers.

Aortic Aneurysm

Nature of Abdominal Aortic Aneurysm

Abdominal aortic aneurysm refers to the dilatation or expansion of the aortic wall due to degenerative or inflammatory destruction of the components of the wall. The vast majority of abdominal aortic aneurysms are due to atherosclerosis, although other conditions, including infection, trauma, dissection, or inherited metabolic disease (Ehlers-Danlos syndrome) may be causes. The dilatation may involve only a portion of the arterial wall (saccular aneurysm), but most often involves generalized fusiform enlargement of the artery. Most abdominal aortic aneurysms are located distal to the renal arteries and proximal to the aortic bifurcation. Abdominal aortic aneurysms may coexist with aneurysmal changes in the iliac, femoral, or popliteal arteries. Less commonly, an aneurysm may involve the entire aorta, including the suprarenal and descending thoracic aorta (thoracoabdominal aneurysm).

Most abdominal aortic aneurysms are asymptomatic and are discovered incidentally during a physical examination or on X-ray examination of the spine or abdominal organs. Symptoms, such as back pain or shock, are usually associated with the complication of rupture and constitute the main threat of abdominal aneurysm. Less commonly, distal embolization may lead to acute or chronic peripheral arterial occlusive disease. Although palpation of aortic enlargement is the best clinical indicator of abdominal aneurysm, abdominal B-mode ultrasonography is the most accurate noninvasive method to estimate the exact size of the aneurysm. Arteriography is seldom used before an operation unless there is associated occlusive peripheral vascular disease or a suspicion of renovascular hypertension; this is because the arteriogram may often not depict the true size of the aneurysm owing to the mural thrombus contained within the aneurysm. Surgical repair with a prosthetic graft is recommended for all abdominal aortic aneurysms more than 5 cm in diameter unless associated diseases make the operative risk greater than that of the prognosis of the aneurysm. The risk of rupture increases exponentially with the diameter of the aneurysm.

TABLE 2.—Mortality ratios and deaths (n in parentheses)[1] from nonsyphilitic aortic aneurysm related to smoking, prospective studies, United States

Author and year	Number and type of population	Data collection	Follow-up years	Number of deaths	Cigarettes per day	Pipes	Cigars	Comments
Hammond and Horn 1958 (*32, 33*)	187,783 white males in 9 States, 50–69 years of age	Questionnaire and followup of death certificate	1.5	66	NS[2] ..... 1.00 (23) (expected) Std[2] ..... 2.73 (66) ($p < 0.005$)			
Kahn 1966 (*40*)	U.S. male veterans, 2,266,674 person-years	Questionnaire and followup of death certificate	8.6	491	>30 ..... 7.36 (66) NS ..... 1.00 (68) Current cigarettes: 8.24 (256) 1–9 cigarettes/day: 2.13 (13) 10–20 ..... 8.33 (124) 21–39 ..... 5.36 (79)	NS–1.00 (68) Std–1.13 (8)	NS–1.00 (68) Std–1.06 (34)	
Hammond & Garfinkel 1968 (*31*)	358,834 males, 448,878 females, 40–79 years of age at entry	Questionnaire and followup of death certificate	6	557	NS ..... 1.00 1–9 ..... 2.03 10–19 ..... 2.56 20–39 ..... 4.54 >40 ..... 8.00			Data apply only to males, 40–69 years of age
Weir and Dunn 1970 (*59*)	88,153 California male workers, 35–64 years of age at entry	Questionnaire and followup of death certificate	5–8	61	NS ..... 1.00 All ..... 2.84 ≤10 ..... 2.44 ≥20 ..... 2.86 ≥30 ..... 2.54			Std includes ex-smokers; NS includes pipe and cigar smokers

[1] Unless otherwise specified, deviations between the total number of deaths and the individual categories are due to the exclusion of nonsmokers, miscellaneous, or former smokers.
[2] NS = nonsmokers; Std = smokers.

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Summary of Epidemiologic Data

Several large epidemiologic studies have suggested an elevated incidence of death from ruptured abdominal aneurysm in smokers compared with nonsmokers (*31, 32, 33, 45, 85*) (Table 2). Anderson et al. (*1*) analyzed 344 autopsies for causes of death and relationship to smoking history. The male to female ratio was 1.9:1.0, with a smoking incidence of more than double that of the general population. The overall longevity of men was less than that of women. There was an inverse relationship between smoking and longevity. Five diseases that accounted for 39 percent of the deaths of smokers were bronchogenic carcinoma, peptic ulcer, aortic aneurysm, acute myocardial infarction, and centrilobular emphysema. The 15 ruptured abdominal aortic aneurysms were in 13 male and 2 female smoking patients.

Auerbach and Garfinkel (*4*) evaluated atherosclerosis and aneurysm of the aorta relative to smoking habits and age. In 1,412 aortas collected at autopsy from 1965 to 1970 from male patients, there was a direct relationship between the extent of atherosclerotic lesions and both smoking habit and age. The aortic lesions were graded for formation of plaques, ulceration, and calcification. The complexity of the plaques increased with the number of cigarettes smoked and was greater in ex-cigarette smokers and pipe or cigar smokers than in nonsmokers. More extensive alterations were found in the abdominal aorta than in the thoracic aorta. Aneurysms were found eight times more frequently among those smoking one to two packs of cigarettes per day than among nonsmokers. Black subjects showed about one-half the number of aneurysms and fewer extensive atherosclerotic lesions than did white subjects. At ages over 65 years, abdominal aortic aneurysms were found in 11 percent of all men and in 16 percent of the heavy smokers.

Rogot and Murray (*64*) evaluated the smoking relationship to causes of death among U.S. veterans. Over a 16-year period, there was a significant reduction in mortality rate with the number of years of smoking cessation. Aortic aneurysm, along with bronchitis and emphysema and lung cancer, were among the diseases in which substantial excess risk remained even after 20 years' cessation of cigarette smoking.

Conclusions

1. Cigarette smoking is the most powerful risk factor predisposing to atherosclerotic peripheral arterial disease.
2. Smoking cessation plays an important role in the medical and surgical management of atherosclerotic peripheral vascular disease.
3. Death from rupture of an atherosclerotic abdominal aneurysm is more common in cigarette smokers than in nonsmokers.

52649 4557

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To: Dr. Alan Rodgman
From: J.H. Robinson
Re: Critique of "Smokers of Low-Yield Cigarettes Do Not Consume Less Nicotine"

7/25/83

The above mentioned paper is basically a sound scientific study. In particular, the cotinine determination method is a published and accepted one. One of the few criticisms of this method is that it involves a multiple extraction procedure which can be subject to contamination from a number of sources. However, in the methods paper describing the extraction procedure (enclosed), the authors are well aware of this drawback and seem to control for it adequately by carefully handling all samples/glassware during the extraction procedure. The cotinine determination is in all probability sound.

The paper itself expresses what we in Biobehavioral have "felt" for quite some time. That is, smokers smoke differently than the FTC machine and may very well smoke to obtain a certain level of nicotine in their bloodstream. If a given level of nicotine in the blood is the final goal of a smoker, one would predict that he would smoke an FFT and ULT cigarette differently. If the smoker could obtain the same nicotine in his bloodstream from an FFT and ULT cigarette by modifying his puffing/inhaling pattern, it would be expected that the blood cotinine level would be the same after smoking either cigarette on a regular basis. This all falls under the area of smoker compensation which we have been interested in studying for some time now.

About the only serious criticism that could be leveled at this paper is that not enough is really known about the pharmacokinetics of nicotine and cotinine to determine if the data presented here are 100% accurate. The authors admit on pg. 140 that cotinine is not a perfect marker for nicotine intake "but we have no reason to think that there is any relation between rate or pattern of nicotine or cotinine metabolism and the brand of cigarette smoked that would cause our data to be biased." This however is unknown. Nicotine is known to effect the metabolism of many therapeutic drugs. It is not known whether the level of nicotine ingested effects its own metabolism. (In the dog this is apparently the case). It is possible (though unknown) that high nicotine injectors (FFT smokers) might metabolize nicotine differently than low nicotine ingestors (ULT smokers). If this is the case, it could have profound effects on the cotinine levels measured in these two categories of smokers.

Finally, the data reported in this paper remind us of the HMSM experiment done with the German Camel and Marlboro cigarettes. While there were certain imperfections in this experiment, you may recall that the smokers apparently obtained almost exactly the same amount of nicotine no matter which of the four cigarettes they smoked. This was one of the first indications that smokers may in fact smoke to obtain a certain level of nicotine in their bloodstream. Data like these make me feel that the data reported in this current publication are probably correct.

J.H. Robinson

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Smoker Compensation Review Draft 4/15/83

I. Introduction

With the advent of lowered 'tar' and nicotine delivery cigarettes, the notion developed that people modify their smoking habits depending upon the type or delivery of the product smoked. This notion is often termed "smoker compensation" or "compensatory smoking behavior". A body of research has been performed in which various aspects of the compensation phenomenon have been studied. This review is not intended to be an exhaustive survey of the scientific literature. Rather, it is a review of the types of behaviors people might use to compensate, ways in which the behaviors have been measured and the impact of the behaviors on cigarette delivery ranking schemes.

II. Compensatory Behaviors

A multitude of factors influence cigarette 'tar' and nicotine deliveries. The cigarette design has a large influence. Ventilation and efficient filtration systems are used to produce low delivery cigarettes. The manner in which cigarettes are smoked also governs the deliveries. This includes the size (volume) of the puff, the duration and frequency of puffing and the amount of the cigarette left after smoking (butt length). In standardized cigarette testing, the product designs are fixed, as well as the exact way the products are smoked. Currently, the FTC uses a standard smoking test which accounts for the puff volume (35 ml), duration (2 sec) and puffing frequency (60 sec). The test methodology provides a means to test the various cigarettes on the market and provide a relative ranking of the per cigarette deliveries of 'tar' and nicotine.

When people smoke, they can alter the deliveries of cigarettes by changing the way the cigarette is smoked. A wide range of puff volumes can be taken. Puffs can be taken with varying frequency and duration. It is also possible for smokers to vary the number of puffs taken as well as the length of unused "butt".

Puffing patterns will be different for different individuals. In addition, a given person may use different puffing patterns each time a cigarette is smoked. For example, while one is relaxing, most of a cigarette may smolder in an ashtray while in times of stress, one may take relatively large puffs in rapid succession. Variations in puffing parameters are even possible during the smoking of a given cigarette. One large puff could be taken, followed after several minutes by a small one, followed by a succession of several puffs of varying volumes taken over a time span of less than a minute.

Since a finite amount of tobacco is available in a cigarette for consumption during smoking, puffing patterns must interact to a degree. A smoker cannot take a few small puffs very rapidly and end up with a short "butt", for example. Likewise, it is improbable that very great numbers of very large puffs could be taken with long intervals between them. Thus, the interactions of the elements of puffing patterns can serve to limit the ranges of the elements. Even so, the ranges of volumes, frequencies, durations, numbers of puffs and "butt" lengths usable by smokers can be impressively great.

In addition to adjustment of the way a cigarette is smoked, people

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can actually alter the cigarette itself. Most cigarettes now sold include a filter. The filter or a portion of it can be removed prior to smoking. Many current cigarettes incorporate vents in the filter for the purpose of reducing the delivery of 'tar' and nicotine. These vents can be blocked by covering them with the lips, fingers or with tape. Filter removal and vent-blocking are examples of cigarette manipulations which will increase the deliveries of 'tar' and nicotine.

Other cigarette manipulations can be performed to reduce the 'tar' and nicotine delivery. The filter or tobacco portion can be pierced to provide ventilation. Mouthpiece devices are available (e.g., "One Step at a Time", "Aqua-Filter") which increase the ventilation level. Cigarette holders which provide additional smoke filtration can also be used.

A range of conditions for usage of cigarette manipulations can be envisioned. A smoker who removes a cigarette filter may do so with every cigarette, or with one or two per day. Similar usage patterns for cigarette holders are possible as well. Blockage of vents could be done on every cigarette, a few cigarettes or even a few puffs on a single cigarette.

The smoking behaviors discussed thus far have dealt with means to modify the deliveries of 'tar' and nicotine from cigarettes. That is, smokers can adjust the amount of smoke which exits the cigarette by changing the way they smoke and by altering the cigarette. The amount of smoke which exits the cigarette can be termed "exposure" and is the amount of smoke available for inhalation by a smoker. This "exposure" to smoke is not the same, then as smoke "dosage". The term "dosage" means the amount of smoke inhaled and taken into the body.

The distinction between "exposure" and "dosage" is an important one. Currently, the FTC standard method accounts for puffing patterns which influence smoke deliveries. Since the same puffing patterns are used for all cigarettes, and the patterns are not necessarily representative of "human smoking", the method provides a relative ranking of deliveries of various cigarettes. These rankings indicate the relative "exposure" to smoke, if the cigarette were smoked exactly as defined by the standard method. To determine smoke "dosage", the smoke "exposure" and the portion of smoke taken into the body must somehow be accounted for. Estimation of smoke "dosage" requires knowledge of inhalation patterns as well as the responses of smokers' bodies to inhaled smoke. Thus, "dosage" estimation requires information on variables beyond that required for an "exposure" ranking. Further, since inhalation and individual responses to smoke must vary widely among smokers, dosage estimation is considerably complex.

Smokers can adjust smoke dosage by altering inhalation patterns. The smoke can be taken into the mouth and held, without inhalation. Some of the smoke can be "released" from the mouth prior to inhalation. Depth of inhalation can also vary as well as the time the smoke is held in the lungs. In addition to varying inhalation patterns, the smoker can change the number of cigarettes used per day. As with puffing patterns, a range of inhalation and cigarette usage patterns can be envisioned. A given smoker may or may not inhale each puff from a cigarette. The number of cigarettes smoked will vary from day to day.

In summary, there is a variety of "compensatory behaviors" available

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which can be utilized to alter the smoke delivery of cigarettes and the dosage of smoke. It is emphasized that all factors discussed above vary over a wide range. Further, each of the behaviors discussed are interrelated and several of the factors discussed can occur simultaneously. For example, a smoker could modify his puffing pattern so that a high 'tar' delivery was obtained, but limit his smoke dosage by not inhaling the smoke. This behavior could be evident for one or all cigarettes smoked by the individual over a given time span. Thus, the smoking behavior model is complex. Many factors must be accounted for to determine the actual smoke "delivery" and even more information must be available to ascertain the "dosage" of smoke.

III. Measurement of Compensatory Behavior

Measurement of human smoking characteristics has been of interest to researchers for almost 50 years. Initially, the primary reason for study was to gather puff volumes, durations and frequencies for use in "realistic" machine smoking tests. More recently, studies of human puffing characteristics have centered on how much smoke people get from cigarettes and how the smoke is inhaled. Two types of studies have been used. These are observation of smokers either in or outside the laboratory and direct measurement on cigarettes smoked by persons in controlled laboratory conditions.

Several studies have been conducted in which observation of smokers was used to estimate puff frequency, duration, number of puffs and butt length. Usually, studies of this type employ covert observation. However, in some studies, smokers were aware they were under observation. In observational studies, criteria are established to define a puff. These might include the time the cigarette is in the mouth, or the time the coal is glowing. This amount of time is measured and taken as the durations. Observers time the intervals between puffs so defined and count the numbers of puffs. Sometimes, the spent cigarette "butts" are collected as well.

The advantage of observational studies is the ability to estimate puffing characteristics in "natural" settings. There are several disadvantages. It is difficult for the observer to determine exactly when a cigarette is being puffed. This uncertainty makes estimation of durations, frequencies and numbers of puffs prone to a degree of error. Puff volumes cannot be measured by observation. Rather, averages of puffing frequency, and duration are used to machine-smoke cigarettes at varying volumes until observed numbers of puffs or butt lengths are obtained. The volume at which this "match" is achieved is taken as the average smoker puff volume.

Table I summarizes results of some observational studies done between 1957 and 1979. Note the wide disparity between numbers of puffs, puffing frequencies and (where available) puff durations. These discrepancies are due in part to subject populations and testing conditions. Particularly noteworthy are the large differences in puff durations reported by two researchers (1.92 vs 4.4-5.4 sec). Differences of this nature are due to the different criteria for visual establishment of "a puff" and the difficulty in objective measurement of timing.

Direct measurement of puffing patterns has also been performed. In these cases, the cigarettes are fitted with instruments to record the

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puff volumes, durations and frequencies. The number of puffs taken can also be obtained. The advantage of direct measurement is that precise and objective volume and timing data can be obtained. Instrumentation has advanced to the state that highly accurate measurements can be made. The major disadvantage associated with these direct measures is that cigarettes must be instrumented and smokers must be asked to participate in experiments. The setting in which the participants smoke, as well as any activities performed in addition to smoking has been found to influence the puffing patterns observed, particularly the puffing frequency.

Table II sumarizes some results of direct measurements of puffing patterns done between 1933 and 1979. A different measurement technique was used in each of the experiments shown. Over the time span from 1933 to the present, the measurement techniques have advanced. This advancement of technology may account for a slight increase in observed puff volumes observed over the years. Disparities in observations might also be due to widely varying experimental conditions such as subject populations, cigarette smoked and setting in the laboratory. It is interesting to compare the puffing frequency data in Table I ("realistic" smoking) to that in Table II ("laboratory" smoking). Data in Table I indicate that cigarettes were puffed 0.8 to 1.7 times per minute. Direct measures (Table II) show from 3.2 to 1.5 puffs taken per minute. Although part of the difference is due to experimental technique, it is probable that the smoking setting ("natural" vs laboratory) accounts for a major portion of the discrepancy.

No large body of research has been performed on smoker behavior regarding cigarette manipulation. The idea of cigarette manipulation is not new, however. The patent literature contains several disclosures including adjustable filters, cigarette "piercing" devices, ventilation and filtration holders or mouthpieces meant to be sold separately from cigarette products. Each of these devices is designed to decrease the 'tar' and nicotine deliveries of any cigarette product. Measures to indicate usage of these devices could be made by obtaining self-report data and/or sales figures for devices which are on the market. To determine the impact of usage of such devices on smoke deliveries, measurements would have to be made while smokers were using the devices. Studies of the extent of usage have not yet been done, but at least one study has been done of the changes in some puffing parameters that occur when different ventilating holders are used. In this case, numbers of puffs and puffing frequency were measured for 3 subjects smoking instrumented cigarettes with cigarette holders which provided 4 increasing levels of ventilation. Both number of puffs and puffing frequency were shown to increase with increasing ventilation (18). The smokers participating in the study did not normally use the cigarette holders, however. Thus, it is not known whether smokers of a given brand who normally use holders exhibit elevated numbers of puffs and frequencies relative to smokers of the same brand who do not use the holders.

Examples of cigarette manipulation behaviors which increase deliveries include filter removal and blockage of air dilution vents. No studies have surfaced which indicate the extent or impact of complete removal of the filter prior to smoking. Such a study would rely on self-disclosure of tendency to remove the filter, coupled with smoking patterns of people who exhibit this behavior.

Vent-blocking behavior has been studied briefly by researchers at

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RJ Reynolds (Report to FTC on Barclay 2/14/82) and by Dr. L.T. Kozlowski (17). Techniques used for measurement included smoker interviews, observation of smokers during smoking and visual analysis of staining patterns on spent filters. In the RJR study, it was found that observation of smokers produced unclear results due to uncertainties in determining exactly when a puff was taken and whether the filter vents were blocked by smokers' lips or fingers at that time. Smoker interviews can only give information about smokers who knowingly block vents. Kozlowski (17) reported that staining patterns on used filters and observation of smokers indicated more extensive vent blocking than would be shown from smoker interviews. These data led Kozlowski to speculate that smokers unwittingly block vents. However, each of the methods for observing vent blocking behaviors reported to date can give ambigous results. For *** these reasons, speculations are premature at this juncture.

Increasing or decreasing the number of cigarettes smoked per unit time is a method smokers can employ to alter total smoke uptake or "dosage". Self-report data on cigarette consumption is included in many studies of smoking behavior. For several reasons (i.e., image, guilt, memory), the self-report data is not completely reliable. Improved measures can be obtained from sales and smoker population data. Consumer Reports ("The Ultra-Low Tar Gimmick",p.27,Jan,1983) reported that the number of smokers (in the US) increased by 3% between 1965 and 1980, but the number of cigarettes consumed increased by 19% over the same period. Coupled with the fact that sales of "ultra-low" 'tar' cigarettes have increased over the years, it would appear that consumers are smoking more as deliveries decline. Recent sales and smoker population data do not support the assumption. These data (RJR research) show that among smokers of filtered cigarettes, high 'tar' (32.4 cig/day), middle 'tar' (31.5 cig/day) and low 'tar' (33.8 cig/day) consumers smoke about the same number of cigarettes. Interestingly, people who use non-filtered cigarettes smoke more than any other category (36.2 cig/day). Obviously, the simple model of "less 'tar'--more cigarettes" is simplistic at best.

note to counsel. data above are from MDD. they may be confidential.

Another means to alter intake or smoke dosage is to vary the actual inhalation of smoke. Direct measurements of the timing of inhalations in relation to puffing patterns of smokers have been performed. Estimates of inhaltion volumes have also been made. Indirect measures of inhalation of smoke are concerned with determination of "markers" of smoke in the body. Cotinine (a metabolite of nicotine) and nicotine have been measured in blood and urine of smokers. Carbon monoxide has been determined in expired breath and in blood as carboxyhamoglobin. Direct measures of inhalation patterns are made with instruments attached to the smoker and must necessarily be done in the laboratory. Measures of biological "markers" of smoke must be made in the labora- *** tory as well, but smoking can be done in natural settings. In studies where smoke "markers" are measured, subjects are asked to smoke a particular cigarette for a given time span and periodically return to the laboratory so that blood or urine samples can be taken. Problems can arise in these studies in that it is not known with certainty if the subjects actually used the test cigarettes, and that the researchers cannot control other variables (i.e., diet, environment) which might *** also affect the measurements.

Although measurements of smoking behaviors have been made with a

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variety of techniques over a rather long time span, the state of the art is still advancing. As apparent from the above overview, one of the problems in studying smoking behavior is the wide array of possible behavior patterns. As a result of technical problems with instrumentation and experimental designs, the available literature presents only a fragmented model of smoking behavior, replete with conflicting results (e.g., Tables I and II). Still, advanced instrumentation has enabled good measurements of puffing volumes, durations and frequencies. Although technically reliable, puffing pattern measurements have been observed to be affected by the laboratory setting in which the experiments were conducted. Thus, the greatest utility of puffing pattern measurements is in comparisons between identical experimental conditions. Reliable methods are also available to estimate the numbers of cigarettes smoked by consumers. To develop a better understanding of smoking behavior, improved methods for observation of vent blocking and other cigarette manipulations are required. In addition, improvements to methods for measuring inhalation and smoke "markers" in the body are needed before smoke dosage estimation becomes possible.

IV. Ranges of Observations of Compensatory Behavior

Typically, experiments in which puffing patterns are measured fall into two categories. In the first, observations or direct measures have been performed while subjects smoked only one type of cigarette. Summaries of results of this type of experiment are shown in Tables I and II. Results of direct measures of puffing patterns (Table II) show good consistency since 1962, even though subjects and cigarette types studied vary widely. These data indicate that the puffing patterns used by smokers are different from current FTC standards, i.e., the puff volumes are higher (~45 ml vs. 35 ml), the puffs are more frequent (~35 sec vs 60 sec), but the durations are similar. A major discrepancy exists between estimates of puffing frequency made with instrumented cigarettes (Tables II,III,IV) and those obtained from observation of smokers in environments outside the laboratory (Table I). The discrepancy indicates that the smoking environment can influence puffing frequency results. In fact, frequencies estimated via smoker observation are typically about one half (e.g., less frequent) those obtained in the laboratory by direct measurement. In one study (Table I, ref. 5) puffing was found to be less frequent when subjects smoked while engaged in "social conversation" with an observer than when not. In another study (Table III, RJR data), direct measurements of puffing frequency were made while smokers were engaged in working jigsaw puzzles and while they did nothing but smoke. Puffing was not as frequent when the smokers were involved with working the puzzles. These results indicate that the impact of the smoking environment on puffing pattern data must be considered when interpreting or designing experiments of this nature.

The second category of experimental designs is one in which subjects smoke a control cigarette, then cigarettes of higher or lower deliveries. The control cigarette is either arbitrary or the subjects' usual brand. Results of some direct measurements of puffing patterns obtained with this type of design are shown in Table III. The data show that when nominal cigarette deliveries are decreased, either puff volumes or puffing frequencies or both increase. Interestingly, three studies (13,15,16) were performed in Great Britain. These used cigarettes with high (by US standards) 'tar' yields, but the puffing pattern results were roughly comparable to those found by RJR for smok-

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ers of lower yield cigarettes (2 mg - 14 mg FTC 'tar') in the US. This would appear to indicate that American smokers might use lower puffing frequencies and volumes if given the 16 mg to 36 mg 'tar' cigarettes employed in the other studies.

Each of the "brand switching" studies summarized in Table III evaluated puffing patterns on a short-term basis. That is, comparisons were made between smoking patterns used at one 'tar' delivery and those used at another, arbitrary 'tar' delivery by smokers who were not habituated to one or the other 'tar' level. Some measurements of puffing patterns of subjects smoking their usual brands (high, middle and low FTC 'tar') are shown in Table IV. These data are in qualitative agreement with brand switching studies (Table III). That is, people who smoke lower 'tar' products use slightly higher puff volumes and puff more frequently than smokers of higher 'tar' products. This trend appears to be true for habitual and short-term smoking of low-'tar' brands.

An important feature of puffing pattern results is the extreme variability of each parameter. Volumes, durations and frequencies vary from puff to puff and from smoker to smoker. The variability is so extreme that overall averages of puffing parameters are probably not representative of the behavior of any single smoker. Averages of puffing parameters are sufficient, however, to indicate that smokers consistently alter puffing patterns based on the nominal cigarette delivery.

Attempts to measure "smoke dosage" via biological markers are usually designed in a similar fashion to the puffing pattern measurements. That is, subjects are given cigarettes of one 'tar' delivery to smoke, measurements of the marker are made and the cycle repeated for cigarettes of other 'tar' deliveries. Results of these studies are conflicting and generally are not corrected for variations in puffing habits for the different cigarettes involved. Some data suggest that nominal nicotine delivery and blood cotinine levels are linked. Techniques and experimental designs need additional improvements before general conclusions can be drawn.

V. Impact of Known Compensatory Behavior on Cigarette Rankings

Based on the results of studies similar to those summarized above, it has been stated that low-'tar' smokers use their cigarettes differently than smokers of higher-'tar' products. Different "usage" includes propensity to block vents or otherwise manipulate the cigarette, increasing the number of puffs and the number of cigarettes smoked, puffing more frequently or with larger volumes and inhaling more deeply or holding smoke in the lungs longer. These usage patterns are consistent with the theory that low-'tar' smokers seek to maintain a given nicotine level in the body, regardless of the cigarette. The patterns cited are instances which would tend to increase the "dosage" of nicotine to the smoker.

On the basis of smoker compensation theories, several modifications to the FTC system of cigarette delivery ranking have been proposed. One proposed modification would result in use of "realistic" puffing parameters. Another would use different puffing parameters for cigarettes in different delivery categories. Yet another proposal involves blocking vents on low-'tar' cigarettes during the smoking test. Rankings based on biological markers have also been proposed. Finally, consumer warnings to the effect that deliveries depend on smoking hab-

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its, have also been advocated.

Evidence is available to lend support to the contention that smokers' puff volumes are higher, and puffing is more frequent than currently specified in the FTC machine smoking test. Further, different puffing patterns have been observed for smokers of low- and high-'tar' cigarettes. If these differences were incorporated in the standard test method, cigarette deliveries would increase relative to current FTC results. If different smoking patterns were used for low- and high-'tar' products, deliveries of some low-'tar' products would increase relative to those found for the higher-'tar' brands. The extent of the delivery changes would depend on the puffing pattern or patterns used as "standard(s)".

Use of amended puffing patterns in machine smoking tests does not make the delivery ranking system more "realistic". Even if the best data available were used to establish new test conditions, it would not be possible to indicate the tremendous range of influence the smoker can exert on cigarette deliveries. Rather than providing a "better" or more "realistic" cigarette delivery indicator, revised smoking parameters can only result in another relative ranking system, like the current test, but with numerically higher 'tar' and nicotine rankings for most, if not all brands.

Scant experimental results exist to support alterations to the FTC method to account for cigarette manipulations. Insufficient data are available to suggest how often, by what means and with what brands vent-blocking or other forms of cigarette manipulation are used by smokers. Even so, vent-blocking has been singled-out as a smoking behavior which should be accounted for in standard delivery ranking tests. If the goal of a cigarette smoking test is to provide realistic indication of actual deliveries to smokers, all forms of manipulations which influence deliveries would have to be accounted for. As in the case of revised puffing patterns, accounting for cigarette manipulation would not improve the realism of delivery rankings. The likely result of test revisions to account for vent-blocking or other manipulations would be changes in the delivery results for the cigarettes that were "manipulated" in the test. The resulting rankings would remain a relative indicator of cigarette deliveries.

Rankings based on measurement of biological markers of smoke in humans (e.g., cotinine) have been suggested. The results of such measures indicate the dosage of smoke to people and not the delivery of smoke from the cigarette. Thus, cigarette rankings derived from biological testing would indicate the responses of individuals to smoke and not the relative differences between cigarettes, based on a standardized smoking protocol. Although techniques for measurement of biological smoke markers are improving, controversy in the scientific community still exists over exactly how studies should be conducted and what the results mean. Even with totally reliable methodology, it is doubtful that routine periodic testing of over 200 cigarette brands could be accomplished due to the cost and complexity of the experiments. If practical and technical difficulties were solved, "dosage" measurements would result in another type of relative ranking of differences between various cigarettes. That is, every smoker and every condition could not be tested and thus, the rankings would be no more "realistic" than other testing schemes.

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Modification to the FTC smoking test to achieve "realistic" cigarette delivery rankings is an impossible task. The FTC and the tobacco industry have always known that no "standard" test could accurately estimate deliveries to humans. Too many variables are involved. Research on smoking behavior has only defined some of the variables. Even if all facets of smoking behavior were known and quantified, some averaging process would have to be used in order to account for the behaviors in a "standard test". Since only averages could be managed, relative rankings would ultimately result and individual smokers would have no better information on their particular "delivery" or "dosage". In view of these facts, the only responsible action is to educate consumers regarding the meaning of the current FTC delivery rankings.

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Table I. Covert and Overt Observations of Puffing Patterns

Year (ref.)	number of subjects	number of puffs	puff duration (seconds)	puff frequency (puffs/minute)
1957 (1)	92	12		1.05
1959-61 (2,3)	94	11.4		1.06
	154	14.0		1.17
	46	14.6		1.22
1968 (4)	21	9.1	1.92	1.10
1974 (5)	30	6.6	4.36	0.79[a]
		7.4	5.41	0.90[b]
1970 (6)	36	13.05		1.74[c]
		9.27		1.02[d]

* Subjects in the study were aware they were observed.

a "Social" smoking, e.g., observers engaged the subjects in non-smoking related conversation during smoking.

b "Non-social" smoking, e.g., observer was present during smoking, but did not converse with subjects.

c "low nicotine" cigarette

d "high nicotine" cigarette

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Table II. Results of Direct Measurement of Puffing Patterns

Year (ref.)	number of subjects	puff volume (ml)	puff duration (seconds)	puff frequency (seconds)
1933 (7)	7	42.5	~2	~30
1937 (8)	10	32	1.5-2.0	~30
1957 (9)	20	37.4	1.58	----
1959 (10)	--	25-40	----	----
1958 (11)	83	24.4	1.7	19.0
1962 (12)	120	43.7	1.91	31.5
1968 (13)	20	47.5	2.20	37.3
1972 (14)	~500	43.5	2.12	27.9

* time from the beginning of one puff to the beginning of the next

Public Health Cigarette

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Table III: Puffing Pattern Changes with Different 'Tar' Deliveries

cigarette (ref.)	number of puffs	puff volume (ml)	puff duration (seconds)	puff frequency (seconds)
"usual",21mg	12	38.5	1.85	42.6
test,16 mg	14	38.5	2.35	42.6
(15)				
mid-'tar'	10	44.1	2.1	34.2
low-'tar'	10.2	55.3	2.4	36.6
(13)				
high-'tar',36mg	---	39.6	2.14	38.6
mid-'tar',23mg	---	44.5	2.35	39.9
low-'tar',16mg	---	53.4	2.77	40.0
(16)				
high-'tar',14.3mg	---	43.7	2.00	35.4
mid-'tar',12.9mg	---	45.3	1.80	29.7
low-'tar',2.0mg	---	45.6	1.59	16.3
(RJR data,a)				
high-'tar',14.3mg	---	41.3	1.69	45.2
mid-'tar',12.9mg	---	47.6	1.66	55.4
low-'tar',2.0mg	---	45.6	1.58	25.1
(RJR data,b)				

* time from the beginning of one puff to the beginning of the next

a Subjects smoked without any task to perform.

b Subjects worked jigsaw puzzles while smoking.

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Table IV. Puffing Patterns with Smokers' Usual Brand

	'tar' delivery		
	a high	b mid	c low
puff volume (ml)	43.5	47.2	47.8
puff duration (sec)	1.70	1.84	1.59
puff frequency (sec)**	28.9	25.1	22.3
number of puffs	12.5	13.1	13.4

a FTC 'tar' was 15 or 15.4 mg, depending upon brand

b FTC 'tar' was 8.2 or 8.6 mg, depending upon brand

c FTC 'tar' was 4.5 or 5.6 mg, depending upon brand

* RJR data.

** Frequency is the time from the beginning of one puff to the beginning of the next.

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KEY ISSUES

#1	SMOKING AND HEALTH CONTROVERSY - GENERAL
#2	ESCALATION OF ANALYTICAL SERVICES
#3	SIMULTANEOUS "TAR" AND NICOTINE REDUCTION
#4	"TAR" REDUCTION, NICOTINE INCREASED OR MAINTAINED
#5	"TAR"
#6	GAS-PHASE COMPONENTS
#7	CLAIMS AGAINST ADDITIVES - CASING MATERIALS AND HUMECTANTS
#8	CLAIMS AGAINST ADDITIVES - FLAVORANTS AND DYES
#9	ENVIRONMENTAL SMOKE
#10	FREON 11 AND EXPANDED TOBACCO
#11	TOBACCO SUBSTITUTES

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KEY ISSUE #1: SMOKING AND HEALTH CONTROVERSY - GENERAL

- RATIONALE:

  THE SMOKING-HEALTH CONTROVERSY WILL CONTINUE AT LEAST AT ITS PRESENT LEVEL.

- IMPACT/IMPLICATIONS:

  - CONTINUED HARASSMENT OF THE TOBACCO INDUSTRY BY GOVERNMENTAL AND MEDICAL AGENCIES ON ALLEGEDLY HARMFUL EFFECTS OF "TAR" AND SPECIFIC COMPONENTS THEREIN, NICOTINE, GAS-PHASE COMPONENTS, ENVIRONMENTAL SMOKE, ETC.
  - EXPONENTIAL INCREASE IN SMOKING-HEALTH PUBLICATIONS, MOSTLY UNFAVORABLE TO THE INDUSTRY.
  - SPIRALING DEPARTMENT INVOLVEMENT, ALREADY EXTENSIVE, IN PROVISION OF SCIENCE INFORMATION TO RJRT, RJRTI, DOMESTIC AND FOREIGN LEGAL PERSONNEL TO COMBAT SMOKING-HEALTH ALLEGATIONS OF THESE GOVERNMENTAL AND MEDICAL AGENCIES.
  - ESCALATING INVOLVEMENT IN PROVISION OF ANALYTICAL DATA TO MONITOR FTC ACTIVITIES, COMPETITORS' PRODUCTS, ETC. SEE KEY ISSUE #2.

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KEY ISSUE #2: ESCALATION OF ANALYTICAL SERVICES

- RATIONALE:

  BECAUSE OF EXTERNAL PRESSURE, PRODUCT COMPLEXITY AND TRENDS, ANALYTICAL REQUIREMENTS WILL MORE THAN DOUBLE BY 1983.

- IMPACT/IMPLICATIONS:
  - COMPLEXITY OF RJRT'S NEW LOW "TAR"/LOW NICOTINE AND LOW "TAR"/MEDIUM-HIGH NICOTINE PRODUCTS AND BRAND EXTENSIONS WILL ESCALATE FTC "TAR"/NICOTINE MONITORING PROGRAM ON PRODUCTION START-UP, MAINTENANCE OF PRODUCT SPECIFICATIONS.
  - SIMILAR MONITORING WILL EVENTUALLY BE NECESSARY FOR PRODUCT CANDIDATES IN CARBON MONOXIDE, NITROGEN OXIDES, HYDROGEN CYANIDE, ACROLEIN, HYDROGEN SULFIDE, ETC. DEVELOPMENT AND UTILIZATION OF HIGH-SAMPLE LOAD ANALYTICAL PROCEDURES TO DETERMINE THESE COMPONENTS ON THE SAME SMOKING SAMPLE AS THE FTC "TAR" AND NICOTINE.
  - DETAILED SMOKE AND TOBACCO BLEND ANALYSES WILL BE REQUIRED IN EVER INCREASING NUMBERS BECAUSE OF THE VARIETY OF SOPHISTICATED RJRT AND COMPETITORS' PRODUCTS DESIGNED TO SATISFY CUSTOMERS WHO BELIEVE SMOKING-HEALTH ALLEGATIONS. THESE PRODUCTS WILL INCORPORATE COMPLEX FLAVORING SYSTEMS AND AIR DILUTION-FILTRATION SYSTEMS, INNOVATIVE BLENDS, UNIQUE FUNCTION ADDITIVES, EXTENDERS, SUBSTITUTES, EXPANDED TOBACCOS, STEM SHEET MATERIALS, COLORANTS, ETC.
  - STRINGENT REGULATIONS BY OSHA, EPA, ETC. WILL ESCALATE DEMAND FOR AIR AND WATER QUALITY DATA.

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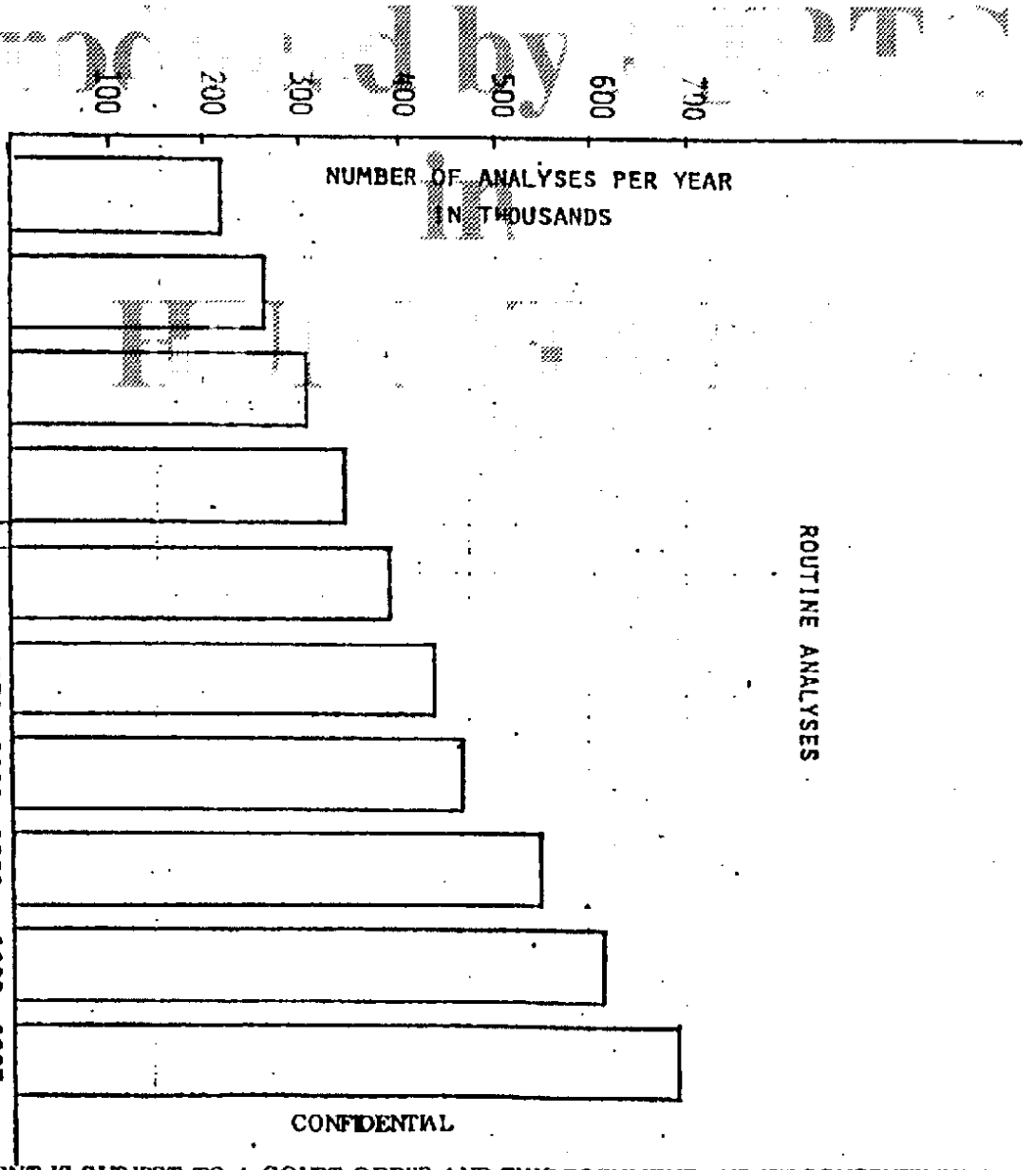

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KEY ISSUE #3: SIMULTANEOUS "TAR" AND NICOTINE REDUCTION

RATIONALE

PRODUCT	SMOKE
CONDEMNATION OF NICOTINE AS HEALTH HAZARD BY SOME SMOKING-HEALTH PROPONENTS; INCREASED DEMAND FOR LOW-NICOTINE TOBACCOS.	SOME SMOKING-HEALTH PROPONENTS ALLEGE SMOKE NICOTINE HARMFUL; SIMULTANEOUS LOWERING OF "TAR" AND NICOTINE RECOMMENDED.

IMPACT/IMPLICATIONS:

- LOWERED "TAR" AND NICOTINE ON ESTABLISHED BRANDS; IF LOWERING OF "TAR" AND NICOTINE PROGRESSES TOO FAR, CUSTOMERS WEANED FROM SMOKING WITH SUBSEQUENT SALES DECLINE
- DECLINE IN SMOKING SATISFACTION IN TERMS OF BOTH FLAVOR AND PHYSIOLOGICAL IMPACT
- COMPLEXITY OF LOW-"TAR"/LOW-NICOTINE PRODUCTS IN TERMS OF BLEND, AIR DILUTION/FILTRATION SYSTEMS, MANUFACTURE, DENICOTINIZATION, ETC. SUBSTANTIALLY REDUCES PROFIT MARGIN
- ADVERSE PR FROM SMOKING-HEALTH PROPONENTS WHO RECOMMEND INCREASED NICOTINE

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KEY ISSUE #4: "TAR" REDUCTION, NICOTINE INCREASED OR MAINTAINED

RATIONALE:

PRODUCT	SMOKE
MANY SMOKERS CONTINUE TO SMOKE DESPITE HEALTH CLAIMS; RECOGNIZING THIS, SOME SMOKING-HEALTH PROPONENTS RECOMMEND LOW- AND MEDIUM-"TAR" CIGARETTES WITH "TAR"/NICOTINE RATIO LESS THAN 8. HIGH-NICOTINE TOBACCO AND/OR NICOTINE SOURCE REQUIRED.	SOME SMOKING-HEALTH PROPONENTS ALLEGE SMOKE NICOTINE HARMLESS BUT "TAR" HARMFUL; SINCE SMOKERS CONTINUE TO SMOKE DESPITE HEALTH CLAIMS, LOWERED "TAR" DELIVERY AND INCREASED NICOTINE DELIVERY RECOMMENDED BY THESE PROPONENTS.

IMPACT/IMPLICATIONS:

- NEW BRAND OPPORTUNITIES IN LOW-"TAR", INCREASED NICOTINE CATEGORY
- SMOKE NICOTINE DELIVERY SHOULD NOT EXCEED THAT IN FULL-FLAVOR CIGARETTES
- DECLINE IN SMOKER SATISFACTION IN TERMS OF FLAVOR BUT IMPROVEMENT IN TERMS OF PHYSIOLOGICAL IMPACT
- ADVERSE PR FROM SMOKING-HEALTH PROPONENTS WHO RECOMMEND DECREASED NICOTINE

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KEY ISSUE #5: "TAR"

RATIONALE:

- "TAR" CONDEMNED BY SMOKING-HEALTH PROPONENTS AS PRIME RISK FACTOR IN SMOKING; PUBLICIZED AT CONTINUALLY INCREASING LEVEL BY ANTAGONISTIC GOVERNMENTAL AND MEDICAL AGENCIES DESPITE FURTHER REDUCTIONS IN "TAR" DELIVERIES.

IMPACT/IMPLICATIONS:

- DECLINE IN SMOKER SATISFACTION (FLAVOR) AND UNIT GROWTH IN INDUSTRY
- CONTINUAL LOWERING OF "TAR" DELIVERY WEANS LIGHT SMOKERS (LESS THAN HALF PACK/DAY) TO QUITTING POINT; LOSS OF SALES
- REALIZATION BY SMOKING-HEALTH PROPONENTS THAT "TAR" NUMBERS GENERATED BY MACHINE SMOKING NOT MEANINGFUL IN TERMS OF HUMAN SMOKING HABITS
- MANDATORY LABELLING FOR "TAR" DELIVERY AT INCREASED PUFF VOLUME

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KEY ISSUE #6: GAS-PHASE COMPONENTS

RATIONALE:

- GAS-PHASE COMPONENTS (CARBON MONOXIDE, NITROGEN OXIDES, HYDROGEN CYANIDE, HYDROGEN SULPHIDE, ALDEHYDES) INDICTED BY SMOKING-HEALTH PROPONENTS AS HARMFUL INGREDIENTS OF MAINSTREAM (AND ENVIRONMENTAL) SMOKE AND PUBLICIZED BY ANTAGONISTIC GOVERNMENTAL AND MEDICAL AGENCIES.
- PREVIOUSLY USED OR NEW FILTER MATERIALS AND COMPONENTS EFFECTIVE IN REDUCING MAINSTREAM GAS-PHASE COMPONENTS WILL APPEAR IN RESPONSE TO THESE ALLEGATIONS.

IMPACT/IMPLICATIONS:

- "DERBY" FOR EACH GAS-PHASE COMPONENT
- MANDATORY LABELLING OR REPORTING FOR ALLEGEDLY HARMFUL COMPONENTS; EXTENSIVE INVOLVEMENT OF LEGAL DEPT., R&D DEPT. IN ASSURING CORRECTNESS OF ANALYTICAL AND REPORTING METHODS.
- PROLIFERATION OF CARBON-FILTER BRANDS WITH NO CARBON-FILTER OFF-TASTE, SPECIAL FILTER-ADDITIVE BRANDS, AIR-DILUTED BRANDS WITH CLAIMS DIRECTED AT SPECIFIC GAS-PHASE COMPONENTS
- TREMENDOUS OPPORTUNITY AND ADVANTAGE TO INDUSTRY MEMBER DISCOVERING EFFECTIVE AND PRACTICAL SYSTEM TO CONTROL MAINSTREAM AND SIDESTREAM GAS-PHASE COMPONENTS; UNLESS AIR DILUTION IS USED, MULTIPLE SYSTEMS WILL BE REQUIRED
- PROVISION OF DATA TO DISCOUNT CLAIMS OF ALLEGEDLY HARMFUL EFFECTS OF GAS-PHASE COMPONENTS

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KEY ISSUE #7: CLAIMS AGAINST ADDITIVES - CASING MATERIALS AND HUMECTANTS

RATIONALE:

CASING MATERIALS (SUGAR, LICORICE, COCOA) AND HUMECTANTS (GLYCEROL, PROPYLENE GLYCOL, TRIETHYLENE GLYCOL) USED ON CIGARETTE TOBACCOS WILL BE CONDEMNED BY SMOKING-HEALTH PROPONENTS AS PRECURSORS OF ALLEGEDLY HARMFUL COMPONENTS IN SMOKE.

IMPACT/IMPLICATIONS

- MANDATORY LABELLING ON CIGARETTE PACKAGE
- REFORMULATION OF EXISTING BLENDS
- NEW BRAND OPPORTUNITIES
- SEARCH FOR ACCEPTABLE SUBSTITUTES FOR USE IN PRODUCT AND/OR MANUFACTURING OPERATION
- PROVISION OF DATA TO DISCOUNT CLAIMS

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KEY ISSUE #8: CLAIMS AGAINST ADDITIVES - FLAVORANTS AND DYES

RATIONALE:

- FLAVORANTS, ADDED TO TOBACCO AND/OR FILTER BUT NOT NATURALLY OCCURRING IN TOBACCO OR SMOKE, ALLEGED BY SMOKING-HEALTH PROPONENTS TO INCREASE SMOKE TOXICITY BECAUSE OF THEIR TRANSFER INTACT TO SMOKE AND/OR THEIR DECOMPOSITION TO ALLEGEDLY HARMFUL SMOKE COMPONENTS DURING THE SMOKING PROCESS.
- DYE SYSTEMS USED TO COLOR CIGARETTE OR CIGAR WRAPPER, CONDEMNED BY SMOKING-HEALTH PROPONENTS AS PRECURSORS OF ALLEGEDLY HARMFUL COMPONENTS IN SMOKE.

IMPACT/IMPLICATIONS:

- MANDATORY LABELLING FOR ALL DYES AND FLAVORANTS NOT OCCURRING NATURALLY IN TOBACCO OR SMOKE
- GOVERNMENT INTERVENTION, E.G. FDA, FOR COMPLETE EVALUATION OF ALL FLAVORANTS
- DECLINE IN SMOKING FLAVOR SATISFACTION IF CERTAIN PROPRIETARY FLAVORANTS DELETED FROM COMPANY PRODUCTS
- DEMONSTRATION THAT CERTAIN PROPRIETARY FLAVORANTS ARE INDEED TOBACCO OR SMOKE COMPONENTS.
- LEGISLATION TO PLACE FLAVORANT USE UNDER GOVERNMENTAL AGENCY (FDA)
- LOSS OF PROFIT PROJECTED FROM REPLACEMENT OF LOW-COST TOBACCO TREATED WITH TURKISH-TYPE FLAVORANT FOR HIGH-COST TURKISH; PROHIBITION OF TURKISH-TYPE FLAVORANTS NECESSITATES CONTINUED PURCHASE OF TURKISH
- DEMONSTRATION OF SAFETY OF SPECIFIC FLAVORANTS BY INEXPENSIVE SHORT-TERM IN VITRO TEST (AMES TEST)
- OPPORTUNITIES FOR NEW BRANDS WITH DYED WRAPPER AND/OR NEW FLAVORANT SYSTEMS
- VALIDATION OF DYE SYSTEMS
- REQUIREMENT BY GOVERNMENT AGENCY THAT GRAS LIST FLAVORANTS ARE SAFE ON INHALATION

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KEY ISSUE #9: ENVIRONMENTAL SMOKE

RATIONALE:

ENVIRONMENTAL SMOKE CONDEMNED BY SMOKING-HEALTH PROPONENTS AS HAZARDOUS TO BOTH THE HEALTHY AND AILING NONSMOKER.

IMPACT/IMPLICATIONS:

- INCREASED REGULATIONS ON SMOKING IN PUBLIC PLACES; WORK PLACES, ETC.
- DECLINE IN SALES BECAUSE SMOKER'S CONSUMPTION LIMITED
- OPPORTUNITIES FOR NEW BRANDS WITH REDUCED SIDESTREAM SMOKE COMPONENTS
- MANDATORY LABELLING FOR SIDESTREAM COMPONENTS
- ENVIRONMENTAL SMOKE COMPONENT "DERBY"

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KEY ISSUE #10: FREON 11 AND EXPANDED TOBACCO

RATIONALE:

FORECAST

IMPACT/IMPLICATIONS:

- ALTERNATE EXPANSION PROCESS
- REDUCTION IN USE LEVEL OF FREON 11 EXPANDED TOBACCO WITH ACCOMPANYING REDUCTION IN PROFIT IN BOTH IN-HOUSE PROFITS AND LICENSEE PAYMENTS
- REDUCTION OF RESIDUAL FREON 11 TO LEVEL ACCEPTABLE TO SMOKING-HEALTH PROPONENTS
- COST OF FREON 11 WILL ESCALATE
- RESIDUAL FREON 11 CONDEMNED AS HEALTH HAZARD BY SMOKING-HEALTH PROPONENTS

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KEY ISSUE #11: TOBACCO SUBSTITUTES

RATIONALE:

TOBACCO SUBSTITUTES ENDORSED BY SMOKING-HEALTH PROPONENTS AS EFFECTIVE MEANS TO REDUCE ALLEGED HEALTH HAZARDS FROM SMOKE.

IMPACT/IMPLICATIONS

- COMPETITOR MARKETS CIGARETTE CONTAINING TOBACCO:SUBSTITUTE BLEND
- RJR RESPONDS BY MARKETING CIGARETTE CONTAINING TOBACCO:SUBSTITUTE (J10, CYTREL, OR NSM)
- RJR PROFIT MARGIN SUBSTANTIALLY GREATER THAN THAT OF COMPETITOR BECAUSE OF COST OF J10 RELATIVE TO OTHER SUBSTITUTES (CYTREL, NSM), .. EXPANDED NATURE OF J10

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PROPOSED BIOBEHAVIORAL/BRAND R&D COOPERATIVE PROJECTS

1. Verification of "Desire for Cigarette" (DFC) Testing Method with WINSTON, Marlboro, VANTAGE, Merit, NOW, Cambridge.

2. Correlation of DFC Test Results with Smoking Behavior Measurements and Replicated Human Smokings.

3. Test of CAMEL LIGHT and Merit "Nicotine-Spiked Cigarettes" with DFC, Smoking Behavior Measurements and Replicated Human Smokings.

4. Test of Cigarettes Spiked with D- and L-Nicotine with DFC, Smoking Behavior Measurements and Replicated Human Smokings.

5. DFC Test of Cigarettes with Designed Configurational Changes.

6. Test of MX Products with DFC, Smoking Behavior Measurements and Replicated Human Smokings.

7. Expanded Smoking/Breathing/Blood Nicotine Study of WINSTON and Marlboro Smokers, with Replicated Smokings.

8. Test of Best Available Marlboro Competitor with DFC, Smoking/Breathing/Blood Nicotine Tests, Smoking Behavior Measurements and Replicated Human Smokings.

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PROPOSED BIOBEHAVIORAL/BRAND R&D COOPERATIVE PROJECTS

1. Verification of DFC with WINSTON, Marlboro, VANTAGE, Merit, NOW, Cambridge.

- What is it? - 30 male and 30 female regular smokers, 18-35(?) yrs. old, evenly divided among WINSTON and Marlboro smokers will each smoke each of the 6 target brands, rating DFC and Satisfaction.

- Why do we want to do it? - DFC may relate to amount of nicotine absorbed and also to perceptual factors. Satisfaction may also. Based on previous results, a smoker's regular brand may influence responses to test brands. This must be found out. The test method, once established, will provide a quick readout of how a given cigarette performs versus control brands. In addition, the method will provide a means to find correlations of DFC and Satisfaction with blood nicotine, puffing and breathing behavior and delivered smoke in proposed future work.

- What results are expected? - A direct comparison of several PM & RJR brands with the DFC test. A relatively quick way to evaluate cigarette performance vs. controls will be available. A clarification of the influence of a smoker's regular brand on response to other brands should result. The method can be used with little extra effort in combination with other tests, such as puffing/breathing behaviors and/or blood chemistry.

- When can we begin? - The test method is available. Tests can begin as soon as logistical details are worked out. The test panel is expected to be semi-permanent, so that nearly the same pool of smokers will be available for further tests. Approximately 18 working days will be required for the initial testing of the 6 brands. Analysis of data will require about 7 working days. To meet a target completion date of 4/1/86, testing will have to begin by 2/25/86.

- What resources will be required? -

Site: We recommend that a non-RJR site in Winston-Salem be set on a semi-permanent basis. Cost = ?

Personnel: We recommend that test administrators be contracted.

Subjects: To be recruited by Bellomy Research, Inc. Cost ca. $80 per subject, some previously identified subjects will be available.

Incentive fees: Probably $100 per subject for the whole test.

RJR personnel: Will be required to set up the site, instruct the test administrators, and collate/analyze data. Statistical support will be required for this and other proposed tests.

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2. Correlation of DFC Test Results with Smoking Behavior Measurements and Replicated Human Smokings

o What is it? Thirty male & 30 female regular smokers, 18-35(?) years old, evenly divided among smokers of WINSTON and Marlboro, will each smoke each of the six target brands (WINSTON, Marlboro, VANTAGE, Merit, NOW, Cambridge), rating DFC and Satisfaction. The cigarettes will be equipped with puff profile probes. Replication of the smokings via the human mimic smoking machine (HMSM) will follow.

o Why do we want to do it? Comparison of the DFC and Satisfaction measures made here with results from Experiment 1 will allow determination of how or if the puff profile probes affect these measures. Measurement of smoking behavior will provide data to explore correlations of smoking behavior with DFC and Satisfaction ratings. Replications of the human smoking by HMSM will provide a large base of data on the amounts of "tar" and nicotine actually delivered to consumers by these products. These data will be new and unique. Finally, correlation of the HMSM results with the DFC and Satisfaction ratings will be possible.

o What results are expected? A replication of Experiment 1 will provide additional data with which to evaluate the DFC/Satisfaction measures. Any relationships among DFC/Satisfaction and smoking behavior will be discovered. RJR's first complete data showing actual amounts of "tar" and nicotine delivered to smokers will be obtained. Any relationships among DFC/Satisfaction and actual "tar" and nicotine deliveries will be discovered.

o When can we begin? The DFC/Satisfaction and smoking behavior measurement methods are available. The human mimic smoking machine has been shown to perform adequately. It is essentially ready to go. Establishment of the test site and panel should have been completed in Experiment 1. Assuming that Experiment 1 is complete by April 1, 1986, this second experiment could begin as early as April 7, 1986. Owing to the capacity of the smoking behavior measurement system, approximately 28 working days will be required for the human smoking sessions. Thus, these could be completed by May 14th. Approximately 180 hours of smoking time will be required for

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complete replication of all smokings by the HMSM. This will require about 30 days. Assuming that some of this work can proceed concurrently with the panel work, it could be completed by May 23rd. Data analysis could be complete by June 6th.

What resources will be required?

PANEL MEASUREMENTS:

Site: Semi-permanent, non-RJR site in Winston-Salem.

Personnel: Test administrators will have to include RJR personnel to monitor puff-profile measurement equipment.

Equipment: Equipment for puff-profile measurement is available to accommodate 4 subjects per session. If this can be expanded to accommodate six subjects per session, the time required to execute the panel phase would be reduced to 18 days (i.e. completion of this phase by April 30.). Needed would be two additional transducer arrays @ ca. $1,000/each and modification of software. This last item will require the attention of Mr. Norman. Recommend that semi-automated probe calibrator be constructed ASAP. Host hardware on hand. Design, construction of equipment should be contracted to local engineering firm, cost(?). Recommend that additional probes be made. This requires refurbishment of existing equipment (PTD cooperation required.) Potentially could be done by outside firms (including making of probes.).

Subjects: Sixty-member panel used in Experiment 1. Costs will be inourred for maintenance of the panel by Bellomy Research.

Incentive fees: Ca. $100 per subject for the whole test.

SMOKING REPLICATIONS:

RJR Personnel: HMSM operator-one now available, project that there will be two by the time this experiment begins. (Not a trivial task.)

Equipment: One HMSM available. It is adequate to complete work on projected schedule. Recommend that an additional machine be ordered ASAP. Cost - ca. $10,000. Calibration for second machine will require attention.

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of Dr. Griffith (B/B), Mr. Norman (Brands), and Dr. Sears (Fundamental R&D). Recommend that puff profile monitors be engineered for existing machines and new machine. This will alleviate pressure on computer systems now used, which are same as used for human smoking measurements. Contract to local engineering firms. Cost(?).

Smoke Analyses: "Tar" and nicotine analyses for 3600 ports will be required. CO/CO2 could be done (3600 determinations) but this will require some additional equipment, also.

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3. Test of CAMEL LIGHT and Merit "Nicotine-Spiked Cigarettes" with DFC, Smoking Behavior Measurements, and Replicated Human Smokings.

- What is it? - Nicotine deliveries of CAMEL LIGHT and Merit will be raised by injection of nicotine into filters. Sixty member panel would be divided equally among two or more versions of each cigarette. DFC/Satisfaction ratings would be obtained with uninstrumented cigarettes. Following this, a second round of tests would include simultaneous DFC/Satisfaction and smoking behavior measurements. Replication (HMSM) of these smokings would be done.

- Why do we want to do it? It is known that nicotine delivery can be conveniently manipulated by filter injection. The advantage is that blend and configuration are unaffected. Thus, the potential exists to independently assess the effects of nicotine delivery on DFC/Satisfaction, etc. Separate DFC/Satisfaction and DFC/Satisfaction/Puff Profile experiments are needed to ensure that unanticipated interactions of the spiked-filter and puff measurement techniques do not degrade the quality of the information obtained.

What results are expected? Relationship of blend-independent variations of nicotine to DFC/Satisfaction in FFLT cigarettes. Determination of alteration in smoking behavior and concomitant effects on delivered nicotine and "tar" will be made. Relationship of delivered nicotine and "tar" to DFC/Satisfaction will be obtained.

- When can we begin? - Preliminary work based on machine smoking will be required to determine levels of nicotine to be applied to filters. Effects of short-term aging on nicotine delivery from injected filters will need to be evaluated. This work can begin as soon as Dr. Perfetti is able to do so. Depending upon this work, panel smokings would begin after completion of Experiment 2. This could be as early as May 19th. If only 2 versions of each cigarette are tested, a total of approximately 8 working days would be required to complete both phases of the panel work. Thus, these phases could be complete by July 2nd. Replication of smoking by HMSM could require approximately 60 hours (ca. 10 working days). Assuming completion of Experiment 2's smokings on schedule, this could be

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done by June 13th.

o What resources will be required?

PANEL MEASUREMENTS:

Site: Same as for Experiments 1 and 2.

Personnel: For first phase, non-RJR administrators can be used. For second phase (including behavior measurements) RJR personnel will be required.

Subjects: Same panel as for Experiments 1 and 2. Incentive fees approximately the same.

Cigarettes: Well characterized, stable cigarettes will be required for both panel phases.

Equipment: Puff-profile measurement system will be required for the second phase. It is already available.

SMOKING REPLICATIONS:

RJR Personnel: Same as for Experiment 2.

Equipment: Same as for Experiment 2.

Smoke Analyses: Approximately 1200 single ports for "tar" and nicotine.

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4. Test of Cigarettes Spiked with d- and l-Nicotine with DFC, Smoking Behavior Measurements and Replicated Human Smoking.

- What is it? Sixty member panel divided between two brands, each brand to be smoked unspiked, spiked with d-nicotine and spiked with l-nicotine. All smokers will smoke assigned brand for DFC/Satisfaction alone and then repeat DFC/Satisfaction test with cigarettes instrumented for smoking behavior measurements. Replication (HMSM) of these smokings would then be done.

- Why do we want to do it? Nicotine can occur in two isomeric forms. L-nicotine occurs naturally in tobacco and it is thought that the l-isomer alone is in smoke. In studies of binding of nicotine isomers to rat brain neurons, the l-isomer is much more potent. The d-isomer is expected, therefore, to be much less pharmacologically potent. It has been shown that l-nicotine has sensory value in smoke. The sensory qualities of d-nicotine are unknown. Present methods of chemical analysis do not distinguish the two isomers. Both, if present, would be counted as nicotine.

  Speculation regarding the possible use of d-nicotine in Marlboro and other PM products has been made. One such speculation posits that some fraction of the nicotine in PM products is the d-isomer. It is presumed to have sensory value, but is much less pharmacologically potent. Thus, smokers of these products could experience less pharmacologically-induced effects, while experiencing a "satisfying taste". This might be related to Marlboro's appeal to younger smokers. PM is know to have access to sources of d-nicotine.

- What results are expected? A direct comparison of the effects of d- and l-nicotine on DFC/Satisfaction and smoking behavior. Replication of the smokings will provide data on the amounts of each isomer delivered to the smokers, presuming that a satisfactory analysis can be developed. The results should show whether d-nicotine has value as a smoke component.

- When can we begin? Development of a satisfactory specific determination of d- and l- nicotine would add a great deal to this work, although

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valuable information would be obtained without it. Work to develop this method should be initiated immediately. The schedules of Experiments 1 and 3 should permit the panel phase of Experiment 4 to begin as early as July 20th. This could allow enough time for the d- and l-nicotine analysis to be available. Both panel phases of Experiment 4 could be complete by July 10th. The smoking replications could be completed by July 21st.

c. What resources will be required?

Panel Measurements and Smoking Replications - Essentially the same as for Experiment 3.

Nicotine Analyses - An analytical method for the determination of d- and l-nicotine in each other's presence will be needed. Work should be initiated immediately, either in house or extramurally, on this method.

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5. DFC Test of Cigarettes with Designed Configurational Changes.

o What is it? Three cigarettes with designed configurational changes will be selected by Mr. Norman. DFC/Satisfaction tests will be run on the 60-member panel.

o Why do we want to do it? Previous results have shown that smokers make adjustments to puffing behavior when smoking these products. This test will provide data on how well the products quench the desire to smoke and how "satisfying" they are.

o What results are expected? The results should show whether the configurational changes or shifts in smoking behavior are related to DFC or Satisfaction. This work provides the potential to incorporate these results into mathematical models of the effects of configuration on important smoker reactions.

o When can we begin? Assuming that the second panel phase of Experiment 4 ends on schedule, Experiment 5 could begin on July 20th. Testing should be complete by July 31st. Results should be reportable in early August.

o What resources will be required? Panel testing would be run by contracted administrators utilizing the projected semi-permanent site and the panel as previously described.

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6. Test of MX Products with DFC, Smoking Behavior Measurements, and Replicated Human Smoking.

- What is it? The MX product and two controls(?) would be tested through DFC/Satisfaction ratings of instrumented cigarettes by the 60-member panel. Effects of the puff-profile measurement on the DFC/Satisfaction ratings should have been characterized by previously outlined experiments. Replication of smoking by HMSM would follow.

- Why do we want to do it? The objects of this work are to characterize the responses of smokers to the MX product with the DFC/Satisfaction test, to determine the deliveries of "tar" and nicotine to smokers and to relate the deliveries to DFC/Satisfaction.

- What results are expected? Relative abilities of MX and the controls to quench DFC and provide satisfaction would be determined. These data would relate to the results of Experiment 4, in which the effects of d- and l-nicotine are explored. Smoking replications will provide data on actual deliveries of "tar" and nicotine from MX and the controls. If Marlboro is used as a control and has been shown to deliver d-nicotine, this work could shed light on the importance of this to the potential for success or failure of the MX.

- When do we begin? Depending on the schedule for Experiments 1-5, this work could begin as early as August 4th. The panel smokings could be complete by August 14th. Replication of the smokings by HMSM would require 15 days and could be complete by August 29th.

- What resources will be required? Similar to Experiment 2, except that Experiment 6 is one-half the size.

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7. Expanded Smoking/Breathing/Blood Nicotine Study of WINSTON and Marlboro Smokers.

- What is it? 50-60 male smokers, 21-35 years old, will each smoke WINSTON and Marlboro. The panel will be evenly divided between regular smokers of WINSTON and Marlboro. The cigarette will be instrumented for puff profile measurements. The breathing behavior of the smokers will be monitored with the Respitrace system. Blood samples will be obtained at intervals before, during, and after smoking. Replications of the smokings would be made by HMSM.

- Why do we want to do it? Previous results with 13 smokers indicated that while WINSTON and Marlboro smokers were able to obtain the same amount of nicotine from either cigarette, their smoking/breathing strategies depended upon the cigarette smoked. The proposed test would verify this result in a much larger sample, providing more confidence in the findings. In addition, results from replications of the smokings would relate delivered "tar" and nicotine to the blood nicotine concentration and the smoking/breathing behaviors.

- What results are expected? Confirmation of previous results showing concentration of blood nicotine in smokers of WINSTON and Marlboro. Improved regression relations of puffing/breathing parameters and concentration of blood nicotine. Potential to include actual deliveries of "tar" and nicotine in these relations.

- When can we begin? Assuming completion of Experiments 1-6 on schedule, this work could begin on August 18. Only one Respitrace system is now available, hence only one smoker can be tested at a time. If 50 smokers are to be tested, approximately 42 days will be required to complete all sessions, assuming the success rate is no better than in our original work (60%). If 60 smokers are to be tested, about 50 days will be required. Addition of a second Respitrace system would cut these estimates to 23 days for 50 smokers and 25 days for 60 smokers. It is recommended that an additional Respitrace be ordered ASAP. Assuming the use of one Respitrace with 60 smokers, the human smoking phase could be completed by October 26th. With two systems, this phase could be completed by September 22nd.

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Replicating the smokings by HMSM would require 10 days for the 60-smoker sample.

Assuming that 9 blood samples are taken in each smoking session, 1,080 samples would be generated by 60 smokers. With present analytical capacity, nicotine and cotinine analyses of these samples would require 10-12 weeks. Some analyses could run concurrently with the smoking sessions. If analyses begin the day following the start of smoking sessions, the blood analyses could be finished by November 7th. It is hoped that new equipment to be added by the end of the first quarter will substantially increase (perhaps double) the throughput of the blood analysis method. Assuming this, the analyses would nearly keep pace with the smokings and be finished the week following the last smoking session.

- What resources will be required?

Site: The site will have to be re-configured to accommodate blood sampling and breathing measurements (Cost=?).

Equipment: Enough equipment is on board for the single smoker per session rate. The acquisition of a second Respitrace system will be needed to accommodate 2 smokers per session. This is recommended and will cost approximately $40,000.

Recruitment and Incentives Fees: Thirty to forty additional male subjects will have to be recruited ($2,400 to $3,200). Incentive fees will be $100 per subject ($6,000).

RJR Personnel: A test administrator, puff-profile/Respitrace operator, phlebotomist, and emergency medical technician will be required for the single subject mode. If the two-subject mode is used, an additional phlebotomist will be needed. This could be a temporary. In addition, two persons are required for blood analyses and an HMSM operator will be needed.

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8. Test of Best Available Marlboro Competitor with DFC, Smoking/Breathing/Blood Nicotine, Smoking Behavior Measurements and Replicated Human Smokings.

- What is it? The best Marlboro competitor available from Brand R&D at the end of the third quarter will be used. The 60-member panel will smoke this competitor and the then current Marlboro in DFC/Satisfaction tests and combined DFC/Satisfaction and smoking behavior tests. These tests will be similar to Experiment 1. Replications of human smokings by HMSM from the second of these experiments will be performed. Finally, 30-60 smokers will be used in a test of smoking/breathing behavior and blood nicotine, similar to Experiment 7.

- Why do we want to do it? - This experiment would yield the most complete evaluation possible of the Marlboro competitor that the Behavioral Division could produce. The Marlboro competitor could incorporate features based on knowledge gained in the earlier experiments in addition to features based on Brand R&D's own work.

- What results are expected? Interpretation of the results would be based on the knowledge obtained from Experiments 1-7. The results should show whether features incorporated into the Marlboro competitor are effective and whether their effectiveness can be accounted for on the basis of the measurements made. This would amount to a test of our combined abilities to make effective use of these types of information in a product development effort. In addition, the results could suggest additional improvements to be incorporated in future Marlboro competitors.

- When can we begin? DFC/Satisfaction tests could begin immediately on completion of Experiment 7. Assuming that two products (Marlboro and the Competitor) are to be smoked this will require about 6 days. The combined DFC/smoking behavior tests will require about 10 days. HMSM replications of these smokings will require about 10 days. These could run concurrently with the panel tests. Smoking/breathing/blood nicotine tests would require additional 25-50 days, depending upon the capacity of the equipment as explained for Experiment 7. HMSM replications of these smokings would require another 10 days. Blood analyses for the samples

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will require between 5 and 10 weeks, but can run concurrently with the smokings. The most optimistic schedule could see all tests and analysis completed by year-end. The most pessimistic schedule would see testing and analyses completed in the first quarter of 1987.

What resources will be required? Resources would be similar in nature to those required for one third of Experiments 1 and 2 and all of Experiment 7.

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Subject: Project XB

1. How much nicotine do we need in a 5± mg product to satisfy normal smokers? present date → 0.6 mg Smoke Nic

2. How much free nicotine of the total do we need to get the proper organoleptic feel?

3. What are the limits around the amount of free nicotine before the product is either too harsh or too smooth - ± mg?

4. Do we know the most effective way to add levulinic acid to cigarette to limit amount used and for best control?

   - Effluent from KDN plant yes → preferred
   - Extract from G7 operation yes
   - To tobacco

   How can we assure ourselves that we will have control of process? QA/QC, NIR

5. Can Brad's work help us determine how much free nicotine ~~we need~~ volatile for organoleptic effect? yes

6. How good do we feel that legal group will allow us to sell product we visualize - i.e., take out tar vs add nicotine?

7. Should we look at using tobacco high in nicotine, remove [illegible], add back?

8. Should we be looking at modifying draw characteristics of 5± mg product?

9. What role should ATP group play vs SBU units.

10. What are the opportunities of using this technology in ~~XX~~ and FF products, i.e., WINSTON (XD)?

11. Who should do this work?

12. Do we have enough resources in program, and are we organized most efficiently to succeed (early)?

13. Should we meet at a set time, say biweekly, to review progress (R&D only)?

14. Who should meet - ATP XB Team, Brad, Sam Simmons, John Robinson, Tom Perfetti?

GRD

11/26/90

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12 Functional Teams

A Process
B Chemistry
C Analytical
D Tobacco/Filters
E Aging
F Satisfaction
G Perception
H Acceptance
I Physiology
J Toxicology
K Consumer Panel
L Long Range

36 Personnel

J. Sam Thomasson - A
John McKenzie - A
Tom Brown - A
Dick Haberkern - A
Dan Beeson - A
Lee Williams - A
T. A. Perfetti - B, D, H, L
Fred Best - B
W. Coleman - B
W. Caldwell - B
J. Elder - C
M. Borgerding - C
H. Gordin - C, G, H
Jack White - C
T. J. Porter - D
E. C. Jones - D
J. Redding - D
R. Hayden - D
Lib Villegas - E
J. Robinson - F, G
Bill Needs - F
Margaret Savoca - H
Brad Ingebrethsen - H, I
Amos Westmoreland - H
Mike Dube - H, K
Pat Lippiello - I
Don deBethizy - I
Jim Walker - I
Bob Suber - J
Chris Coggins - J
Chin Lee - J
Dave Doolittle - J
Dave Taylor - J
Cooper Rees - J
Barry Saintsing - B, D, L
Anita Phillips - K, L

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December 5, 1990

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A
PROCESS

1. How get KDN effluent?

2. How add levulinic acid to KDN effluent?

3. How to make HN G7?

4. How to use NS as TD?

5. Manufacturing implementation?

6. Additional sources of nicotine in RJR?

7. Cost analysis?

8. QA methods/SPC?

9. REST?

(JST, TWB, HAE, JLMc, RGH)

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B
CHEMISTRY

1. 1:1, 2:1, 3:1 salts
   - What are the molecular species?
   - Neat, in solution, on tobacco?
   - Equilibrium dynamics, exchange of LA?

2. Fate of NS in a cigarette
   - What ends up in smoke?

3. Comparison of NL to other nicotine salts?

4. Comparison of KDN effluent to pure nicotine

5. Solution dynamics: nicotine concentration needed to form salts?

6. Effect of pH on smoke nicotine yield?

(TAP, FWB, WMC, WSC, BLS)

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C

ANALYTICAL METHODS

1. Levulinic acid in smoke & tobacco.

2. Levulinate salt in tobacco & smoke.

3. Puff x puff TL yields.

4. Free vs. bound nicotine in cigarette smoke/tobacco.

5. Vapor phase vs. particulate phase nicotine determinations.

6. How to enrich nicotine in KDN effluent?
   (in vapor phase)

(HHG, JFE, JLW, MFB)

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D
TOBACCO/FILTERS

1. Which blends are best?
   - RJR signature vs. others

2. What flavor delivery systems to use? TD, Casing

3. Combined filters ?

4. New filter designs?

5. Air dilution ... ent holes?

(JWR, TJP, ECJ, RFH, TAP, BLS)

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E
AGING

1. *Time, Stability?

Process Flow:

KDN effluent

↓

*Concentrated KDN Effluent → Super Conc KDN Eff. → Add Levulinic

↓

Combine with GF extract

↓

Concentrated GF/KDN

↓

Add Levulinic Acid

↓

*Make Sheet

↓

Make Product

(EHV)

*Salts

↓

Top Dress

↓

*Products

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F
SATISFACTION

1. How much nicotine yield as a target?
   (FF, FFLT, ULT smokers vs. product)

2. Physiological endpoint for satisfaction. (EEG)

3. HSB/HMSM/Cluster/DFC

4. Single/multiple smokings ------> blood plasma nicotine

5. Chronic nicotine dose?

(JHR. WAN)

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G
PERCEPTION

1. Effect of draw, burn rate, taste, nicotine, pH, etc. on perceived satisfaction.

2. How do we measure satisfaction?
   - extended use
   - others

3. How much nicotine is required to have perceived satisfaction?
   - [illegible] FFLT, ULT smokers (not product)

(HHG, JHR)

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H

ACCEPTANCE

1. Free vs. bound nicotine (in smoke)?

2. Endogenous vs. surface nicotine?

3. How much levulinic acid required for maximum smoothness?

4. Sheet vs. TD?

5. Is higher nicotine required for XB?

6. How much nicotine required for acceptance?

7. Burn rate, puff count, draw - how maximize for acceptance?

8. Draw - What is it?
   - Temporal effects?

9. Correlation between nicotine & harshness?

10. Effect of nicotine on perceived draw and burn rate?

(HHG, MRS, BJI, AEW, TAP, MFD)

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I
PHYSIOLOGY

1. How does nicotine elicit response?

2. How does levulinic acid elicit response?

3. How does levulinic acid change the response? Same for NL + Na, Ca salts of LA?

4. What is physiological mechanism?
   - [illegible] receptor, trigeminal

5. How does cigarette smoke elicit response?
   - aerodynamics
   - vapor vs. particulate (nicotine/other)
   - pH effects
   - salts
   - LA

6. PB-PK of nicotine and NS

7. Binding studies

(PML, JCW, BJI, JDD)

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J

TOXICOLOGY

1. Chem Tox Plan

2. Safety
   - Handling
   - Processing
   - Manufacturing
   - Trucking/Storage

3. Stewardship of levulinic salts, nicotine levulinic salts, etc.

(WDT, SCR, DJD, CREC, CKL, RLS)

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K
CONSUMER

1. PGT
2. TPT
3. Extended-Use
4. [illegible] Market
5. Optimization
6. Qualitative

(MFD, ABP)

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L

LONG RANGE

(or non levulinic acid approaches)

1. Other ways to raise nicotine or lower tar
   - NaOH filters
   - STT
   - pH modifiers
   - Sanwet
   - Alternate fillers
   - K_2CO_3 (reduce coal temp.)
   - Basic casings

(BLS, TAP, ABP)

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prepared for
in
HUMPHREY

REVIEW OF XGT TECHNOLOGY

PLAINTIFF'S EXHIBIT NO. 30

M. Stowe April 5, 1988

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- Patent Licensing
- T-R&D (X61 technology)

- RJR 02328

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BACKGROUND

The XGT program is an effort to develop technology which will allow RJRT to manufacture reduced delivery cigarettes with smoking characteristics (taste and satisfaction) comparable to products with substantially higher delivery.

If successful, 'tar' and taste/satisfaction will be decoupled and the smoking characteristics of FFLT products can be upgraded to the FF level, those of ULT products an be upgraded to the FFLT level, and (our ultimate goal) the smoking characteristics of ULT products can be upgraded to the FF level.

The GT program made good progress toward the first two goals with use of special tobacco blends. This technology is currently being evaluated in product improvement research in the Existing Business program. Blend technology has not been successful when applied to the larger steps; i.e., ULT to higher end FFLT or to FF.

XGT technology is not limited to use in existing products. Successful development of the technology will provide a tool for use in new generation products also.

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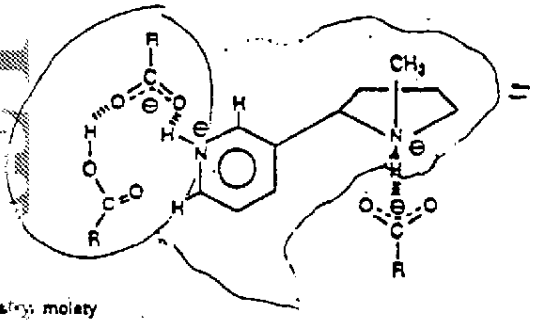
STATUS

Nicotine levulinate is a breakthrough in the development of technology to provide FF taste and satisfaction in ULT products, and development of this technology to a point where it can be employed in an ongoing and/or new brand development program is the R&D objective for the XGT program for 1988.



Nicotine Levulinate

Nicotine levulinate added to reduced delivery products has been shown to increase nicotine delivery significantly without an increase in 'tar' or carbon monoxide, and most significantly without the increase in harshness and throat irritation which has always been found to accompany increases in nicotine delivery relative to 'tar'.

The kinds of increases which have been observed are shown in the following table. These products were described by those who smoked them as very mild. Measurements of plasma nicotine indicate that nicotine uptake is in the range which would be expected from the smoke measurements.

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FTC MACHINE SMOKING DATA

	NOW 85	NOW 85 TEST	WINSTON UL 100	WINSTON UL 100 TEST
'TAR' (mg/clg)	1.80	2.00	4.60	4.90
NICOTINE (mg/clg)	0.18	0.51	0.38	0.81
T/N	10	3.9	12.1	6.0
CO (mg/clg)	2.90	3.10	7.50	6.70

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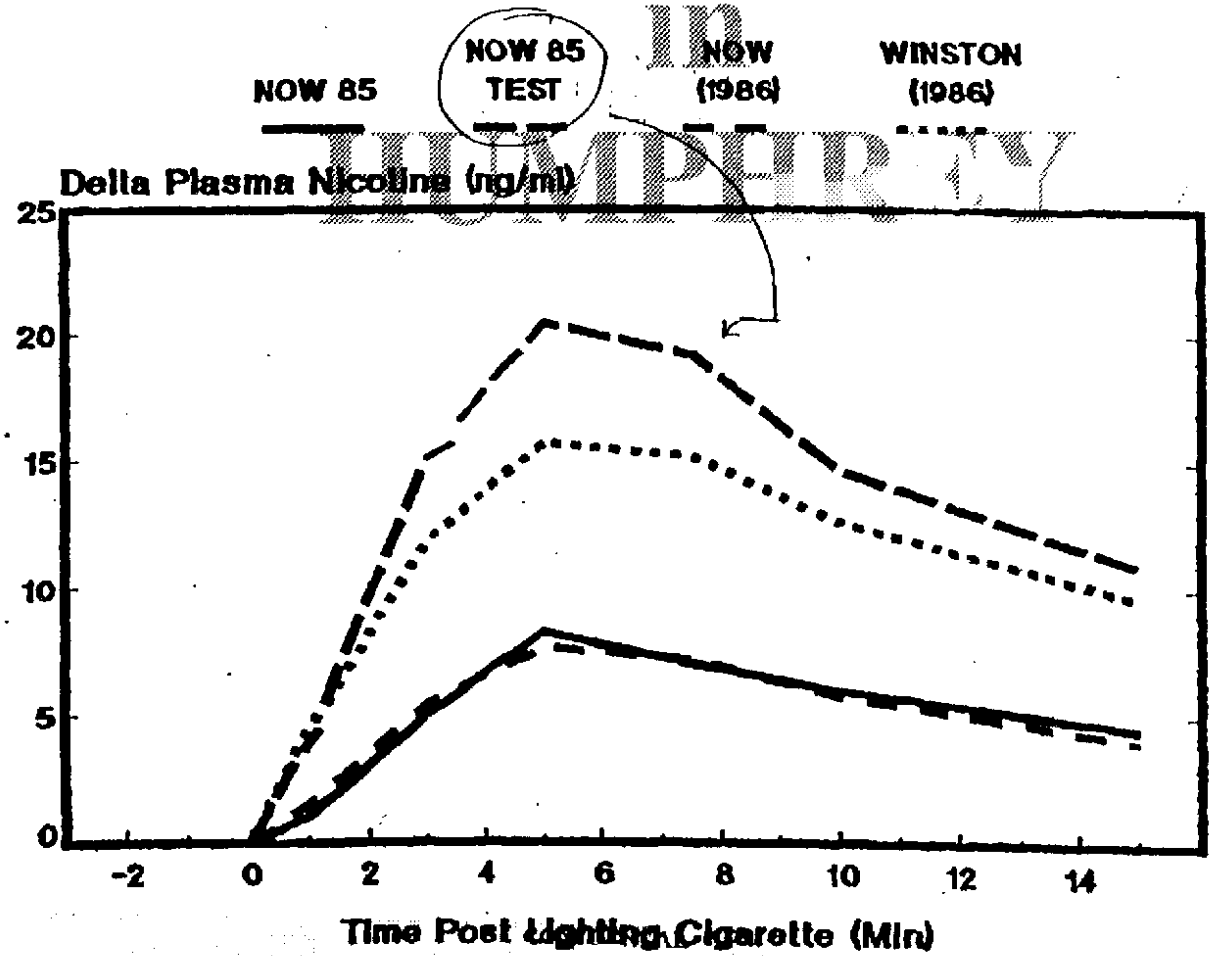
PLASMA NICOTINE "BOOST" (ng/ml)



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1988 PROGRAM

Use of naturally occurring nicotine is desirable. Spray dried tobaccos, tobacco extracts, and otherwise unsmokable high nicotine tobaccos could be potential sources for nicotine. A major goal of the 1988 program is to translate the technology developed with an added nicotine salt to a technology which uses naturally occurring nicotine in combination with an organic acid to control nicotine delivery relative to 'tar'.

A second goal of the 1988 program is to address the extreme mildness of products made with nicotine levulinate. Some flavor enhancement will be needed and this will be sought either through flavor from tobacco extracts or through use of formulated flavors.

1988 Program Plan

Next steps are:

- develop technology which uses spray dried tobaccos or tobacco extracts as a nicotine source,
- combine harshness reduction and flavor enhancement technologies to address the taste reduction which accompanies the harshness reduction,
- develop solid analytical, sensory, and (as indicated) biological data on nicotine control technology,
- evaluate technology in ULT and FFLT products.

Project testing milestones:

- sensory evaluation on test brand (VUL) with extract/levulinic acid technology - 2Q88,
- sensory evaluation of flavor systems - 2Q88,
- consumer evaluation of combined technology (screening) - 3Q88,
- PGT on test brand (VUL) - 4Q88.

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FIRST QUARTER STATUS

* Fourteen different tobacco extracts evaluated at various levels for flavor impact. Four selected for further evaluation.

* Cigarettes prepared for baseline analytical data on delivery of nicotine (from added nicotine levulinate) from various tobacco types.

* Cigarettes prepared for baseline analytical data on use of casing as a carrier for nicotine levulinate.

Next Steps:

* Evaluate nicotine delivery from extracts added to blends and individual tobacco types.

* Complete collection of baseline analytical data.

* Optimize addition of extracts and generate sensory data for use in flavor formulation.

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Weisburger Associates N. White Plains, NY

REPORT OF MEETING

On Friday, August 21, 1987, a meeting was held in Elmsford NY, from 8:30 am to 6:00 pm between John H. Weisburger and the following key professional staff of RJR:

A. Wallace Hayes
Johnnie R. Hayes
William Y. Rice, Jr.
Christopher Coggins
John H. Reynolds
J. Don deBethizy
David J. Doolittle
Michael F. Borgerding
Arnold T. Mosberg
Gary T. Burger

The agenda dealt with a presentation by RJR Staff on research undertaken on comparative toxicological properties of Alpha Product and a reference 1RF4.

In view of the problems associated with the use of the standard smoking products in relation to risk for coronary heart disease, specific types of cancer, emphysema, and related problems in the respiratory tract, RJR has invented a smoking product with a radically new revolutionary design in order to avoid many of the adverse claims associated with conventional smoking products.

The toxicological studies aim to provide the evidence needed to underwrite safety claims associated with Alpha Product.

The use of a standard smoking product involves the combustion of tobacco leading to thousands of chemicals in the mainstream and the sidestream. It is thought that a number of the adverse effects claimed stem from complex interactions of some of these key chemical classes.

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Alpha Product appears to yield about 50% of the CO and carboxyhemoglobin levels compared to the reference material. If the preceding discussion is relevant, one would conclude that alpha product is of lower risk.

The nicotine levels in Alpha Product are also somewhat lower than in many standard products. However, it has been shown with standard cigarettes of varying nicotine output that smokers tend to compensate use pattern in order to ensure certain specific blood level. Your group has performed detailed studies in this area including mechanism studies on pharmacokinetics of infused nicotine. It appears clear that Alpha Product offers the user nicotine in a manner that will be not too dissimilar from that of other cigarettes but at lower levels, yet sufficiently high that the alleged pharmacological requirement is met.

Suggestion for Additional Experiments

The staff has noted a number of spontaneous suggestions that were made during their presentations and ensuing discussions. I will list here a few that are considered relevant that might not have been emphasized during the meeting.

First I would like to reiterate the essence of our conclusions on the desirability of select experimentation on the skin of Swiss mice or other appropriate strain (not Sencar) on the question of initiation and promoting potential of smoke condensates. I should be glad to help design such experiments.

We also noted the desirability in human users to test for the presence of reactive nitrosation potential by giving subjects a pulse of proline and analyzing urine for nitrosoproline. With standard cigarettes, a positive finding has been made. It will be useful to evaluate this particular question with Alpha Product.

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Adverse effects have been associated with the presence of appreciable amounts of polycyclic aromatic hydrocarbons, tobacco specific nitrosamines, and other nitrosamines, reactive nitrosating elements, aromatic and heterocyclic amines, and acidic compounds like phenols, catechols, aldehydes, thiocyanate, and HCN. In great part the presence of these chemicals in the mainstream has been related to adverse effects as regards cancer, emphysema, and respiratory tract diseases. Recently emission of some of these products in the sidestream smoke has been of concern in relation to passive smoking. In addition, standard products emit appreciable amounts of CO, CO2, and nicotine. The presence of CO and in part of nicotine has been thought to be related to an increase risk of myocardial infarction at least in individuals on a Western nutritional tradition.

During our review of the comparative properties of Alpha Product with 1RF4, a number of specific approaches were reviewed. This includes the physical design and combustion properties, the aerosol chemistry, the analytical chemistry, the biological activities in relation to genetic toxicology in vitro and in vivo (urinary mutagens), any promotion effects, limited inhalation experiments in animals short term and up to 90 days as well as physiological and pathological observations. Recently, behavioral smoking patterns, utilizing Alpha Product and a customarily used product, were compared. A number of the experiments to delineate the properties of Alpha Product were conducted not only in house at RJR but also in a select number of highly qualified external contract laboratories. It can be noted that the results obtained in contract laboratories confirmed and extended the results obtained at RJR suggesting a high quality design and performance of tests.

Exacting chemical analyses demonstrate that alpha product yields smoke that is totally different in relation to many components relevant to toxicology compared to reference smoke. Thus, virtually absent is the large class of polycyclic hydrocarbons, of phenols and catechols, and the presence of only small amounts of aldehydes and of the tobacco specific nitrosamines (4 units compared to 130 to 600). Also absent are HCN and thiocyanate. The levels of CO are lower, usually about one half, as are the nicotine levels.

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Detailed studies in cell systems, including those to reveal genetic and promoting effects confirm the absence of significant amounts of chemicals that would be expected to affect such cell systems. Thus the biological effects observed extend the chemical findings.

Inhalation tests in rats on Battelle smoking machines for weeks and for 90 days also gave very little evidence of any physiological and pathological effects of alpha product, whereas such effects were observed with the reference material. Enlargement of the heart was seen in some tests.

The use of Alpha Product by humans provided information about achieved nicotine titers in blood and also showed that users did not excrete any additional mutagens whereas with reference material mutagens were noted in urine.

The considerations outlined above deal mainly with the overall problem of risk for neoplastic diseases and emphysema as studied by chemical and biologic approaches. Approaches to evaluate any risk for myocardial infarction are much more difficult to define mainly because the mechanism whereby smoking of conventional products may lead to this condition has not been defined precisely. Hypotheses suggest that inhaled CO and nicotine or metabolites are involved. It is our view that these agents in turn, exacerbate pre-existing conditions like atherosclerosis in individuals on a typical Western nutritional tradition. Perhaps this is the reason why it has not been possible to design appropriate animal models to mimic this particular effect and approach an understanding of the underlying mechanisms. I am aware of alternative explanations like the singular vascular damage by unknowns in tobacco smoke as a first step in atherosclerosis. I am, however, not impressed with the evidence produced thus far.

Thus, the only current element on which to base a possible risk situation as regards heart disease is the presence of CO measured through carboxyhemoglobin titers, and nicotine levels measured as such or as metabolites.

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file coumarin

MEMORANDUM SECRET

RJR

July 20, 1982

TO: Roy E. Morse

RE: BRITISH BABOON RESEARCH EXONERATES COUMARIN

In 1977 the BAT Research Department in Southampton and Imperial Tobacco Company in Bristol commissioned BIBRA to do a research project on coumarin, using baboons as test animals. The choice of the animals was a deliberate policy decision, based on the knowledge that allegedly the metabolites of coumarin in rats were quite distinct from those in man. This means that BAT and Imperial believe that rat data with coumarin - whether positive or negative - can not be extrapolated to man. The baboon study was run for 24 months; however, serial sacrifices were made, starting at month 16. Coumarin was administered to the animals mixed into their food pellets. The dosages were as follows:

10:	coumarin level as control
2.5mg	per kg body weight
7.5mg	"
22.5mg	"
67.5mg	" (maximum dosage)

The result was that no irregularities were observed at the end of the study. In other words, coumarin was given a completely clean bill of health.

It is important that the fact that we have knowledge of this unpublished study be kept strictly confidential.

At this time it is impossible, or very difficult, for me to obtain additional information. This is mainly because the study was commissioned by both Imperial and BAT, and in order to get real access to the data, it would have to be cleared with both of them. I hope, however, to be able to do this if and when I should go through Great Britain on my next trip to Europe.

The fact that this baboon study was commissioned by BAT/England, with the rationale indicated, makes it all the more incredible that BAT/Germany should have commissioned later the rat study with its questionable outcome. (Please see my memoranda to Mr.Witt, dated March 26, 1982 "German Coumarin Research", and the July 7, 1982 follow-up.)

Frank G. Colby

FGC/ks
cc: S.B.W.
G.R.DiM.
B.F.P.
A.R.✓

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Mr. Max Crohn
Legal Department

Re: Invalidation of Some Reports in the Research Department

We do not foresee any difficulty in the event a decision is reached to remove certain reports from Research files. Once it becomes clear that such action is necessary for the successful defense of our present and future suits, we will promptly remove all such reports from our files.

As a rule, we invalidate about 15 reports each year for various reasons. The most common reasons for invalidating a report and/or requiring rewriting are:

(1) discovery of inaccuracies in data,
(2) erroneous interpretation of data,
(3) purposeless speculation on data,
(4) needless reports of previously reported data and/or discussions,
(5) undue delays in finalizing reports,
(6) confidentiality of contents, and
(7) several miscellaneous reasons.

As to the reports which you are recommending to be invalidated, we can cite misinterpretation of data as reason for invalidation. A further reason is that many of these are needless repetitions and are being removed to alleviate overcrowding of our files.

As an alternative to invalidation, we can have the authors rewrite those sections of the reports which appear objectionable.

We are awaiting a decision as to the action to be taken with respect to the reports in question.

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EXHIBIT
12-4-98 Rodgman

November 16, 1983

The following list of Formal Reports were issued to Alan Rodgman and have been destroyed. Please mark your records accordingly.

1. SOME VOLATILE CONSTITUENTS OF CELLULOSE SMOKE, by James D. Fredrickson. RDR, 1959, No. 35.

2. THE SUTTON RESEARCH CORPORATION SMOKING MATERIAL PART V. INVESTIGATION OF THE SMOKE FROM SUTTON SMOKING MATERIAL, by Charles R. Green, Larry L. Vestal, and Josep[illegible] Schumacher. (Dated January 28, 1969, has no number).

3. THE INVESTIGATION OF THE CIGARETTE SMOKE FROM CELANESE SMOKING MATERIAL, by C. R. Green, L. L. Vestal, J. N. Schumacher. RDR, 1969, No. 32.

4. SMOKE COMPOSITION: L-7661A and L-7081B CIGARETTES, by Charles R. Green. RDR, 1974, No. 10.

5. A RAPID COMPARISON OF SMOKE COMPOSITION OF 50% J-10 AND WINSTON BLEND CIGARETTES, by Robert A. Lloyd and Charles W. Miller. RDR, 1974, No. 12.

6. PYROLYSIS OF J-10: IDENTIFICATION OF LEVOGLUCOSENONE, by R. A. Lloyd and C. W. Miller. RDR, 1974, No. 18.

7. SMOKE COMPOSITION: COMPARISON OF J10 AND J10T SMOKES WITH A TOBACCO CONTROL, by Charles R. Green and Fred W. Best. RDR, 1974, No. 6.

8. SMOKE COMPOSITION: SEMI-QUANTITATIVE COMPARISON OF SMOKES FROM J10-TOBACCO AND TOBACCO CIGARETTES, by C. R. Green, F. W. Best, M. P. Nevell, et al. RDR, 1976, No. 4.

9. SMOKE COMPOSITION: PUFFED VERSUS UNPUFFED TOBACCO BLEND, by C. R. Green and J. N. Schumacher. RDR, 1971, No. 7.

10. SMOKE COMPOSITION: C1-7 BLEND CIGARETTES WITH DYED AND UNDYED OVERWRAPS, by C. R. Green and J. N. Schumacher. RDR, 1971, No. 21.

11. SMOKE COMPOSITION: HOMOGENIZED VERSUS UNHOMOGENIZED TOBACCO BLEND, by J. N. Schumacher, C. R. Green, F. W. Best. RDR, 1972, No. 5.

12. SMOKE COMPOSITION: MTP-DYED AND MTP-CONTROL CIGARETTES, by C. R. Green. RDR, 1973, No. 22.

13. SMOKE COMPOSITION: MTP CIGARETTES L-7137A AND 7137B, by C. R. Green. RDR, 1974, No. 4.

14. SMOKE COMPOSITION OF BURLEY STEMS VERSUS BURLEY TOBACCO, by R. A. Heckman. RDR, 1974, No. 3.

15. SMOKE COMPOSITION: HOMOGENIZED C-7L VERSUS NON-HOMOGENIZED TOBACCO BLEND, by M. P. Nevell, R. A. Heckman, and Charles R. Green. RDR, 1974, No. 4.

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15. FRACTIONATION OF VOLATILE COMPONENTS BY THE TENAX METHOD. PROGRESS REPORT 1, by C. W. Miller and R. A. Lloyd. RDM, 1974, No. 13.

17. SMOKE COMPOSITION: COMPARISON OF THE SMOKE CONDENSATES FROM REGULAR MARLBOROS, OMEGA 100's AND A MENTHOLATED WINCHESTER (L-7254), by C. R. Green and F. W. Best. RDM, 1974, No. 17.

18. SMOKE COMPOSITION: A DETAILED INVESTIGATION OF THE WATER-SOLUBLE PORTION OF CIGARETTE SMOKE, by J. N. Schumacher, F. W. Best, and C. R. Green. RDR, 1974, No. 7.

9. PYROLYSIS PRODUCTS OF LICORICE, by C. R. Green and F. W. Best. RDM, 1974, No. 20.

20. PYROLYSIS PRODUCTS OF VARIOUS SMOKING MATERIALS, by C. R. Green and F. W. Best. RDR, 1975, No. 1.

11. SMOKE COMPOSITION: E-Z CIGARETTES L85277A AND L85278, by R. A. Heckman, M. P. Newell, C. R. Green, C. W. Miller, and F. W. Best. RDM, 1975, No. 24.

22. SMOKE COMPOSITION: COMPARISON OF U.K. MORE (L-9122A) WITH A WHITE PAPER CONTROL (L-9122B), by M. P. Newell, J. N. Schumacher, R. A. Heckman, C. R. Green, F. W. Best, C. W. Miller, A. L. Angel, R. A. Lloyd, G. W. Young, F. A. Thome, and J. M. Martin. RDM, 1975, NO. 42.

23. EFFECT OF TREATMENT OF TOBACCO WITH AMMONIA OR VARIOUS AMMONIUM SALTS ON THE LEVELS OF PYRIDINES AND PYRAZINES IN SMOKE, by C. R. Green, J. M. Martin, and Alan Rozzan. RDR, 1976, No. 3.

16. AN INVESTIGATION OF THE LIPOPHILIC BASES OF CIGARETTE SMOKE CONDENSATE, by R. A. Heckman and F. W. Best. RDR, 1976, No. 3.

25. SMOKE COMPOSITION: COMPARISON OF MORE BLEND WITH TOD-06433 WRAPPER (L-9477A) TO MORE BLEND WITH ECUSTA 856 WRAPPER (L-9477B), by F. W. Best, C. R. Green, R. A. Heckman, C. W. Miller, M. P. Newell, and A. L. Angel. RDM, 1976, No. 15.

26. SMOKE COMPOSITION: I. WINSTON VS MARLBORO, by M. P. Newell, A. L. Angel, F. W. Best, C. R. Green, R. A. Heckman, R. A. Lloyd, C. W. Miller, R. E. Shackelford, F. A. Thome, and G. W. Young. RDR, 1976, No. 9.

27. A COMPARATIVE STUDY OF TOBACCO ESSENTIAL OILS AND ADDITIVES IN MERIT, MARLBORO AND OTHER CIGARETTE PRODUCTS, by R. A. Lloyd, C. W. Miller, D. L. Roberts, and P. H. Ayers. RDM, 1976, No. 21.

28. COMPARATIVE SMOKE STUDIES. II. SALEM VS KOOL, by M. P. Newell, A. L. Angel, C. R. Green, F. W. Best, C. W. Miller, R. A. Lloyd, R. A. Heckman, F. A. Thome, G. W. Young, and R. E. Shackelford. RDR, 1976, No. 10.

29. COMPARATIVE SMOKE STUDIES. IV. G7 CONTROL VS AMMONIATED G7, by M. P. Newell, F. W. Best, C. R. Green, R. A. Heckman, R. A. Lloyd, and C. W. Miller. RDR, 1976, No. 18.

30. COMPARATIVE SMOKE STUDIES. V. VANTAGE VS MERIT, by C. W. Miller, M. P. Newell, and R. E. Shackelford. RDR, 1976, No. 19.

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31. SYNTHETIC SMOKING MATERIALS, by W. Y. Rice, Jr. RDM, 1975, No. 39.

32. MERIT RESEARCH SUMMARY, by Robert A. Lloyd, Jr., RDM, 1978, No. 1.

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